STUDIES ON SEED FATS AND FATTY ACIDS

RESUME

THESIS SUBMITTED FOR THE DEGREE OF

Doctor of Philosophy

IN

Chemistry

SUHAIL AHMAD

DEPARTMENT OF CHEMISTRY
ALIGARH MUSLIM UNIVERSITY
ALIGARH (INDIA)

1984

This thesis consists of two parts: The Part One has three chapters dealing with the compositional studies of minor seed oils and Part Two embodies the work related to the synthesis and characterization of oxygen and sulfur-containing fatty heterocycles.

PART ONE

In continuation of the 'chemical screening program' to explore the oilseed potential of forest flora, a study of seed oils of seven plant species belonging to different families was undertaken for the determination of their fatty acid profile.

1. Minor Seed Oils

Five wild oil-bearing species: *Tephrosia villosa* (Leguminosae), *Bassia* sp. (Sapotaceae), *Polygonum* sp. (Polygonaceae), *Hydrolea zeylanica* (Hydrophyllaceae) and *Lysium barbarum*

(Solanaceae) have been analyzed by using chromatographic and spectroscopic techniques. Seed oils of Bassia sp. and T. villosa are characterized by the presence of (75.8-68.1%) unsaturated acids, a good characteristic of edible oil. The combined oleic-linoleic acid content in the Bassia sp. is extremely rich ($\backsim$ 76%), which resembles somewhat to sunflower seed oil. The two species (Polygonum sp. and H. zeylanica) are found to contain $>$ 25% (37.8 and 28.2%) trienoic (linolenic) acid. The seed oils of L. barbarum and Polygonum sp. contain about 40% palmitic acid. Myristic acid in appreciable amount (7.3%) is also found in Polygonum sp.

2. Hydroxy Fatty Acid in Strychnos potatorum Seed Oil

The seed oil of S. potatorum (Loganiaceae) was found to contain isoricinoleic acid (24.9%). The occurrence of isoricinoleic acid is reported for the first time in this family. The structure of this hydroxy acid was established by various spectroscopic (IR, NMR, Mass) and chromatographic (TLC, GLC) methods.

3. Epoxy Fatty Acids in Siegesbeckia orientalis Seed Oil

The seed oil of S. orientalis (Compositae), which responded to picric test and showed diagnostic spectral data for epoxy acids, has been found to contain 16% coronaric and 4% vernolic acids. The mixture of two epoxy acids was confirmed by TLC

and GLC of the oxygenated fraction of seed oil and mass spectrometry of the methyl ester of the epoxy acids and their methoxy-hydroxy derivatives.

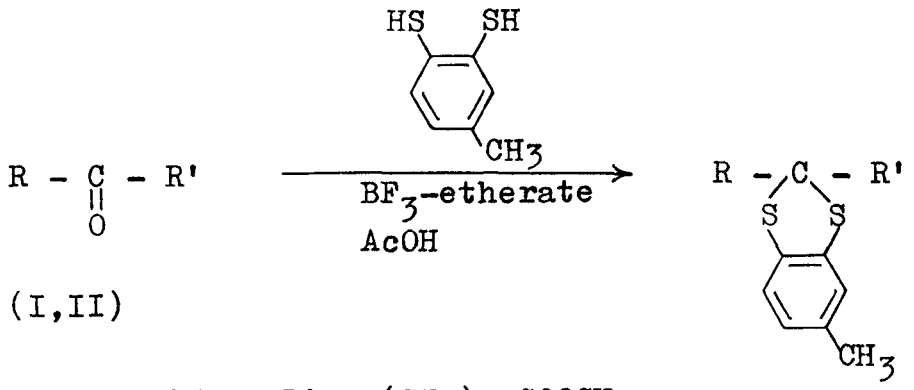
PART TWO

In this part, the chapter 4 describes the preparation and characterization of long chain aromatic dithiolanes, oxathiolanes and dioxolanes from oxo (keto) fatty acids/esters. Palladium-catalyzed alkenylation reaction of methyl 10-undecenoate has been described in chapter 5. The structure of each product has been established on the basis of combustion and spectral data.

4.1 Synthesis of Long Chain Aromatic Dithiolanes

An attempt has been made to prepare aromatic dithiolane fatty derivatives from oxo fatty acids/esters by using toluene-3,4-dithiol, boron triluoride-etherate and acetic acid as the reagent, catalyst and solvent respectively.

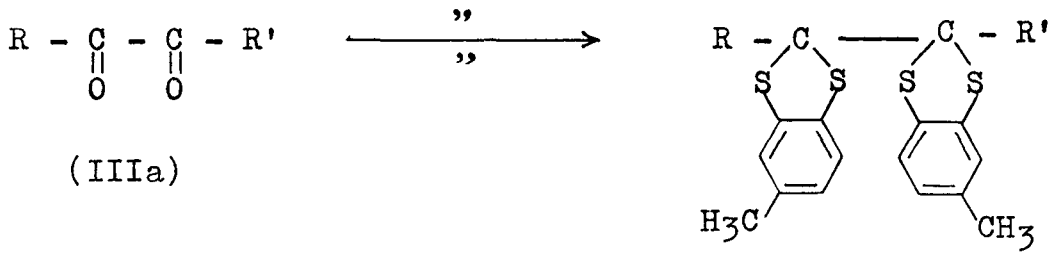
Methyl 10-oxoundecanoate (I), methyl 12-oxooctadecanoate (II) and 9,10-dioxooctadecanoic acid (IIIa) on treatment with toluene 3,4-dithiol yielded dithiolanes (VIII), (IX) and bis-dithiolane (X) respectively in high yields.



(I,II) (VIII, IX)

I, VIII : R = CH_3; R' = $(CH_2)_8$-$COOCH_3$

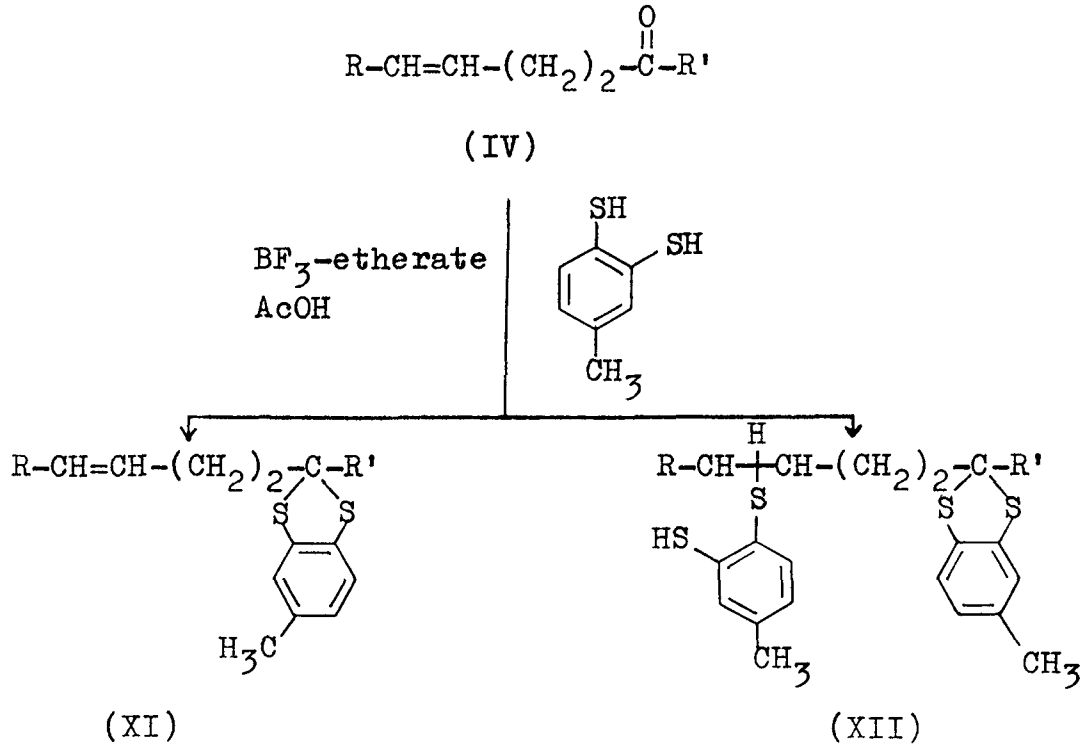
II, IX : R = CH_3-$(CH_2)_5$; R' = $(CH_2)_{10}$-$COOCH_3$



(IIIa) (X)

R = CH_3-$(CH_2)_7$; R' = $(CH_2)_7$-$COOH$

On similar treatment, 9-oxooctadec-cis-12-enoic acid (IV) and 9,12-dioxooctadec-trans-10-enoic acid (V) provided 9,9-toluene-3,4-disulfideoctadec-cis-12-enoic acid (XI) as major, 9,9-toluene-3,4-disulfide-12(13)-[4(3)-thiol toluene-3(4)-mercapto]-octadecanoic acid (XII) as minor; 9,9,12,12-bis-toluene-3,4-disulfideoctadec-trans-10-enoic acid (XIII) as major and 9(12)-toluene-3,4-disulfide-12(9)-oxooctadec-trans-10-enoic acid (XIV) as minor products, respectively. Isomeric nature of the products (XII, XIV) was confirmed by the study of their mass spectra.



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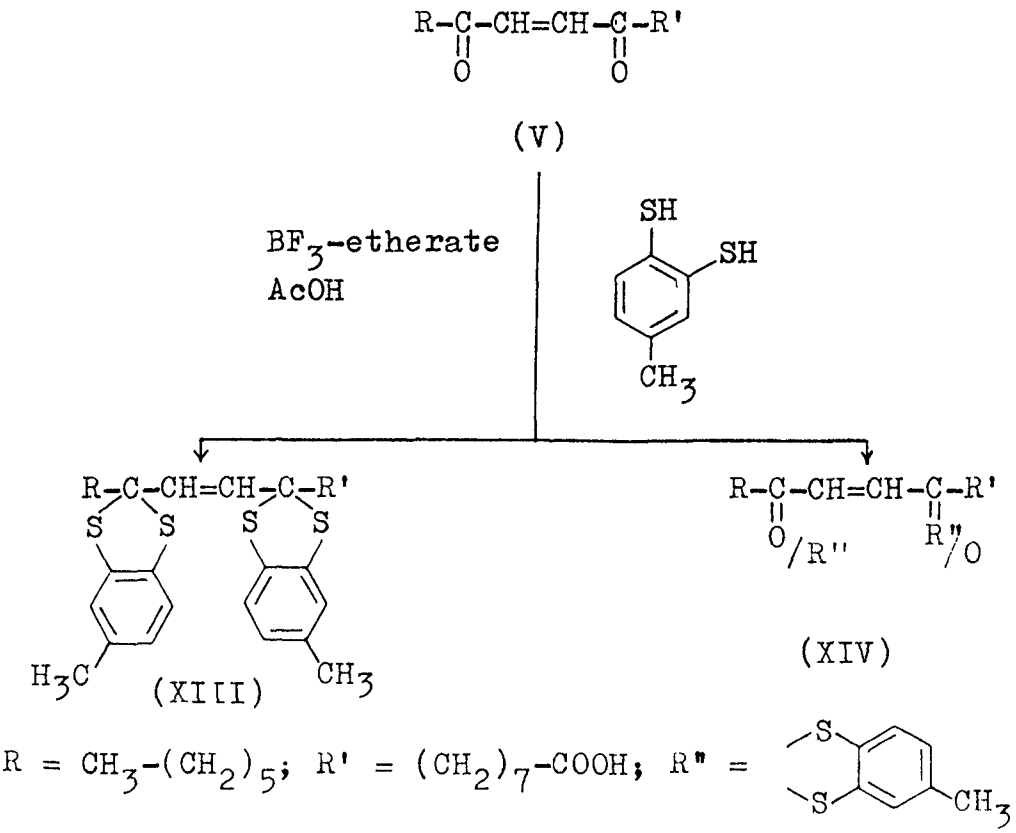
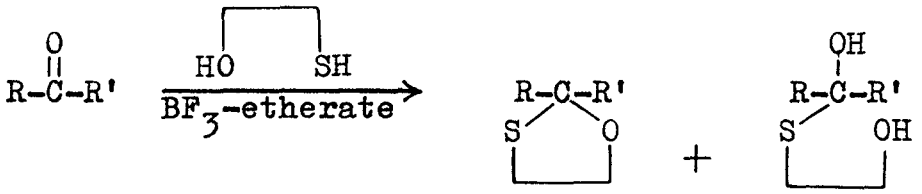


R = $CH_3-(CH_2)_5$; R' = $(CH_2)_7-COOH$; R" =

4.2 Synthesis of Long Chain Oxathiolanes

10-Oxoundecanoic (Ia) and 9-oxooctadecanoic (VIa) acids on reaction with β-mercaptoethanol in the presence of BF_3-etherate afforded oxathiolanes (XV) and (XVII) respectively in good yields along with their corresponding hemimercaptals (XVI) and (XVIII) as the minor products. When methyl 9,10-dioxo-octadecanoate (III) was allowed to react with the same reagent in the presence of BF_3-etherate and acetic acid, it gave methyl 9(10)-(ethyleneoxathiolane)-10(9)-oxooctadecanoate (XIX). Isomeric nature of this product was substantiated by its mass spectral fragmentation pattern. The reactions are depicted in the following schemes.



(Ia,VIa) (XV, XVII) (XVI, XVIII)

Ia, XV, XVI : R = CH_3; R' = $(CH_2)_8$-COOH

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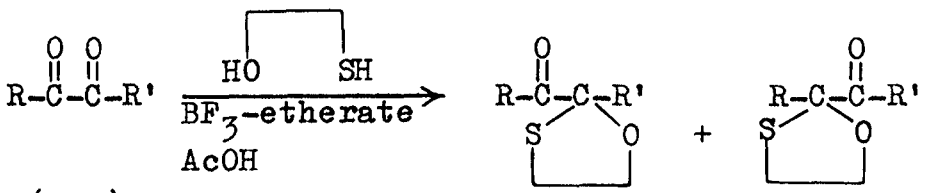
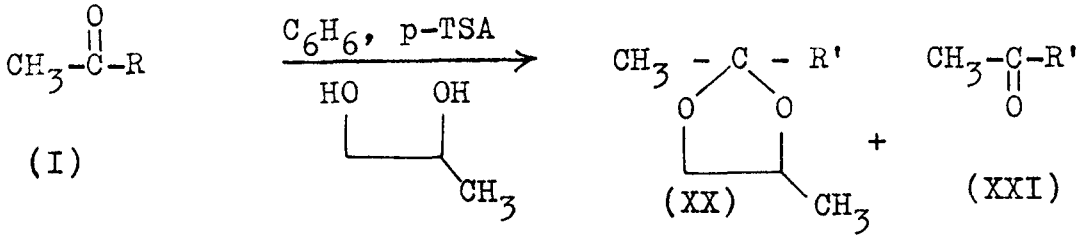


(III) (XIX)

R = $CH_3(CH_2)_7$; R' = $(CH_2)_7$-$COOCH_3$

4.3 Synthesis of Long Chain Dioxolanes

Methyl 10-oxoundecanoate (I) on reaction with the excess of 1,2-propanediol in the presence of benzene and p-TSA provided dioxolane (XX) in 75% yield along with 2'-hydroxypropyl-10-oxoundecanoate (XXI) as a minor product. When methyl 9-oxooctadecanoate (VI) was subjected to the similar reaction conditions, it gave dioxolanes (XXII; 15%) and (XXIII ; 60%) along with 2'-hydroxypropyl 9-oxooctadecanoate (XXIV; 20%). 2-Oxo ester (VII) on similar treatment afforded only one product, 2'-hydroxypropyl 2-(2"-methylethylenedioxolane) octadecanoate (XXV) in 70% yield.



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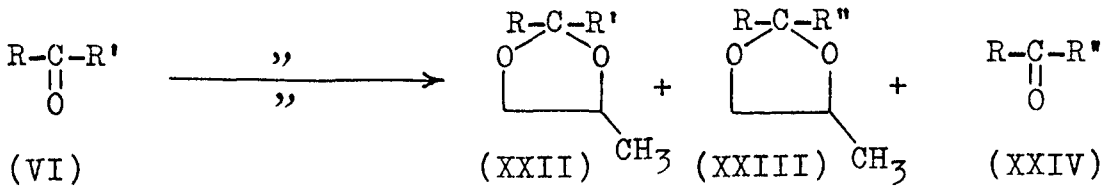
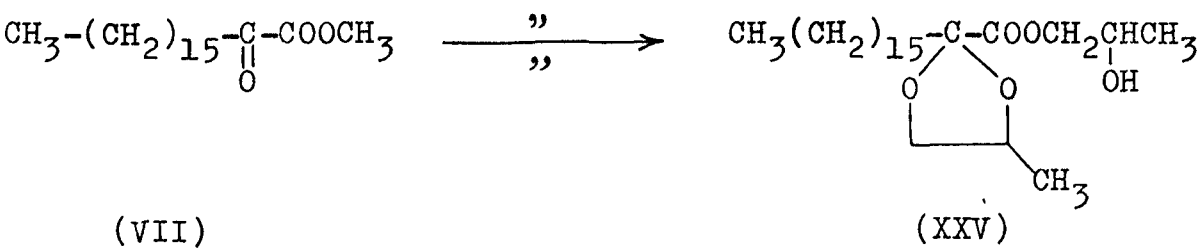
R= $(CH_2)_8COOCH_3$; R' = $(CH_2)_8$-$COOCH_2CH(OH)CH_3$



(VI) (XXII) (XXIII) (XXIV)

R = $CH_3(CH_2)_8$; R' = $(CH_2)_7COOCH_3$; R" = $(CH_2)_7COOCH_2CH(OH)CH_3$



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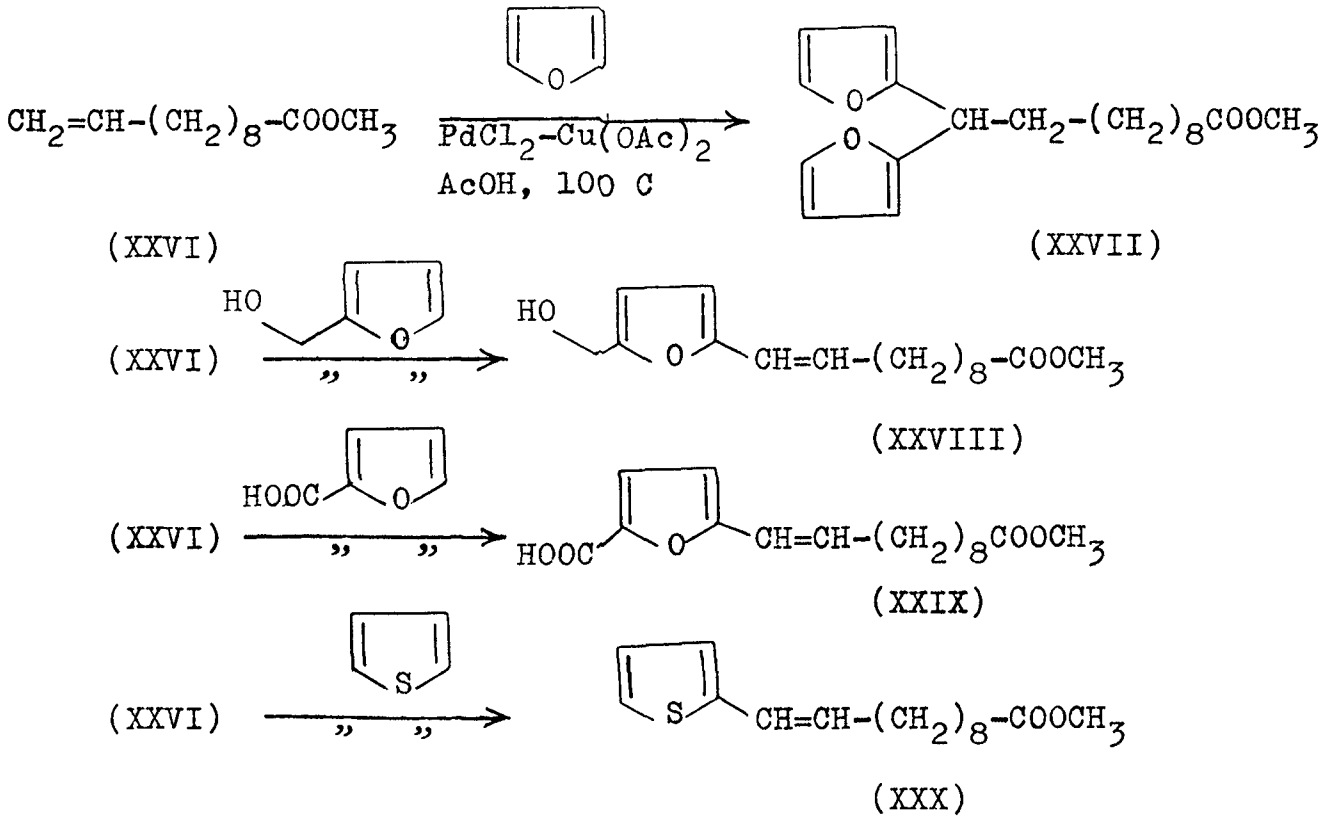
Alkenylation reaction of the terminal olefinic (methyl 10-undecenoate) ester (XXVI) was carried out with furan, furfuryl alcohol, 2-furoic acid, thiophene and pyrrole according to the procedure of Fujiwara and coworkers, using equimolar amounts of $PdCl_2$, $Cu(OAc)_2$, the heterocycles and olefinic ester in a solution of dioxan and acetic acid at 100 C. The corresponding monoalkenylated products were obtained, except with furan and pyrrole. In the case of furan an unusual product (XXVII) was obtained while the reaction did not occur when pyrrole was used.



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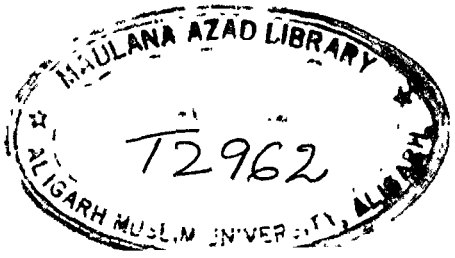
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Dr. S. M. Osman
Professor of Chemistry and
Principal Investigator, PL-480 Project.

Section of Oils & Fats
Department of Chemistry
Aligarh Muslim University
ALIGARH-202001 (India)

Ref. No..... ....

DATE .....30.11.1984..

This is to certify that the work embodied in this thesis entitled, 'Studies on Seed Fats and Fatty Acids' is the original work of Mr. Suhail Ahmad carried out under my supervision. The thesis is suitable for the award of the degree of Doctor of Philosophy in Chemistry.

S.M. Osman

With Love
To
Parents

Acknowledgments

I wish to express my deep sense of gratitude to Professor S.M. Osman for his able guidance and consistent encouragement through out this research work. I am thankful to Professor W. Rahman and Professor M.S. Ahmad, Chairman, Department of Chemistry for providing necessary facilities and useful discussions.

I am greatly indebted to Dr. Fasih Ahmad whose expert knowledge and skill in methodology and anticipation of research problems provided great help to me. I will be pleased to thank all my research colleagues, especially to Dr. Mushfiquddin Khan for their cooperation.

Fine services from instrumentation division A.M.U., Aligarh, R.S.I.C. Lucknow and R.R.L. Jammu, and financial assistance from the Council of Scientific and Industrial Research, New Delhi are gratefully acknowledged.

Suhail Ahmad

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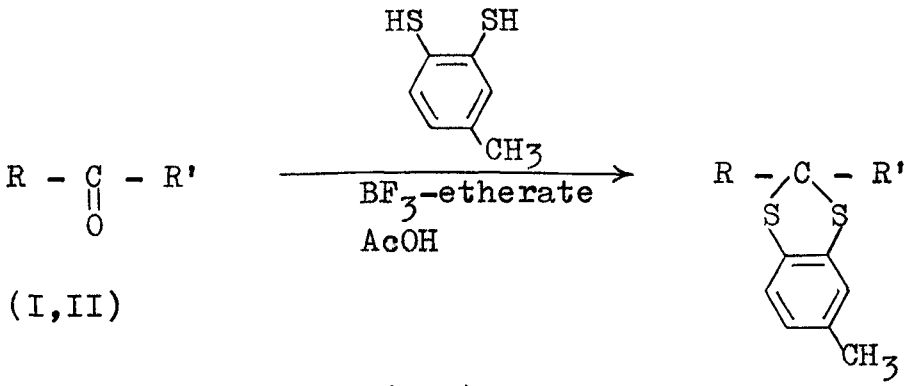

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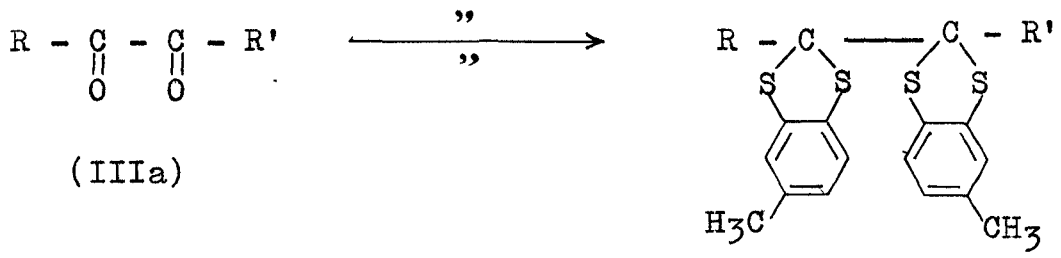

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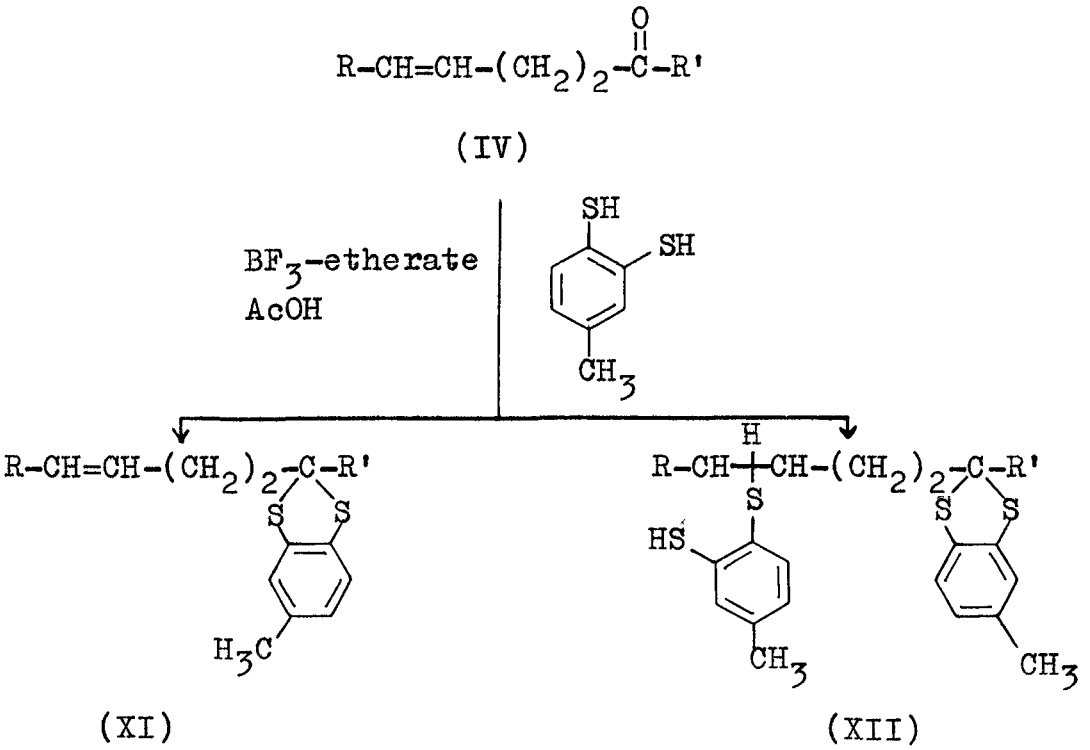

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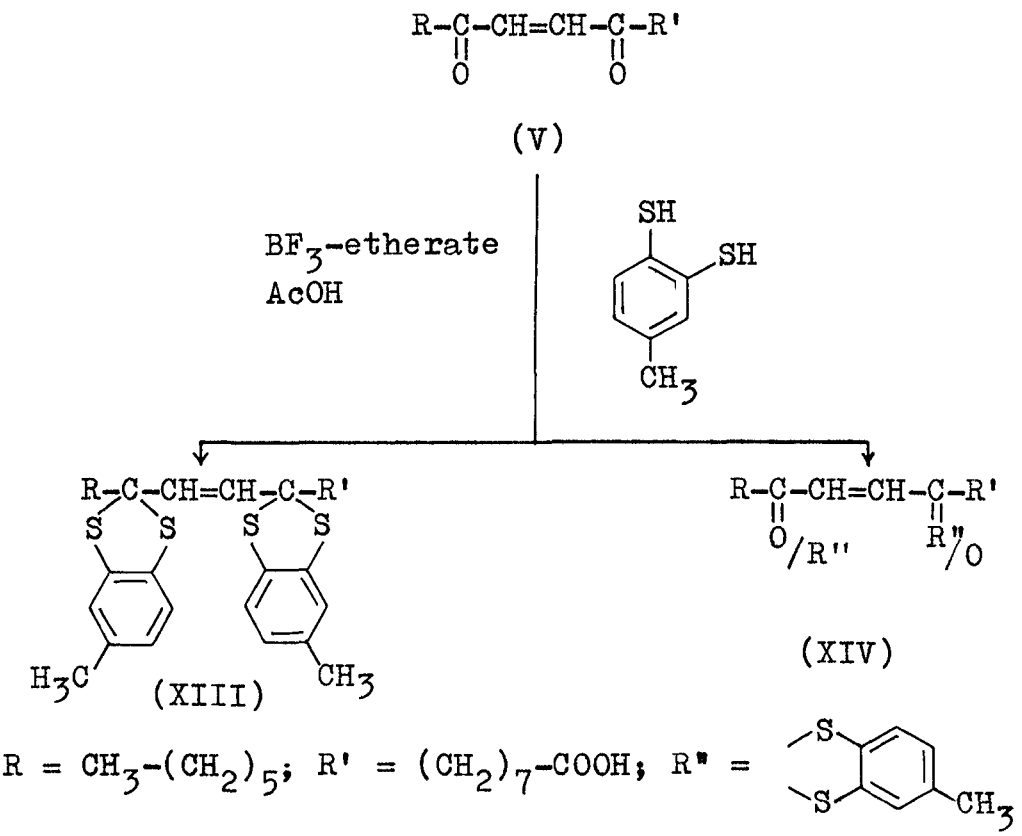

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4.2 Synthesis of Long Chain Oxathiolanes

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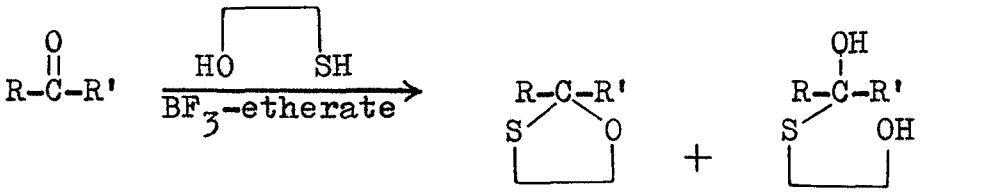

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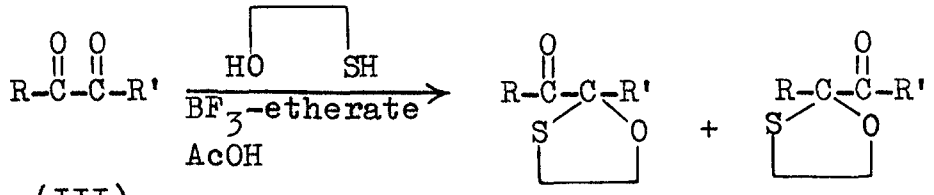

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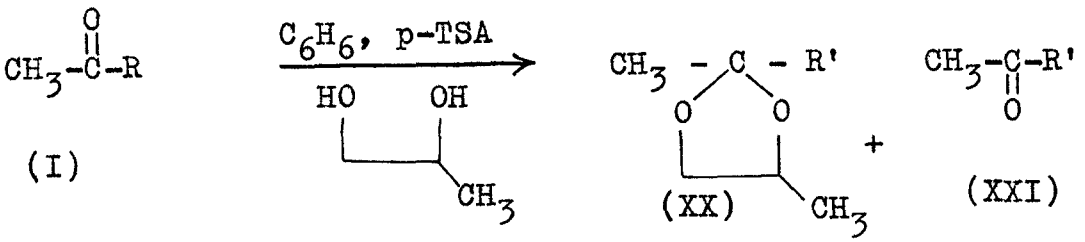
4.3 Synthesis of Long Chain Dioxolanes

Methyl 10-oxoundecanoate (I) on reaction with the excess of 1,2-propanediol in the presence of benzene and p-TSA provided dioxolane (XX) in 75% yield along with 2'-hydroxypropyl-10-oxoundecanoate (XXI) as a minor product. When methyl 9-oxooctadecanoate (VI) was subjected to the similar reaction conditions, it gave dioxolanes (XXII; 15%) and (XXIII ; 60%) along with 2'-hydroxypropyl 9-oxooctadecanoate (XXIV; 20%). 2-Oxo ester (VII) on similar treatment afforded only one product, 2'-hydroxypropyl 2-(2"-methylethylenedioxolane) octadecanoate (XXV) in 70% yield.



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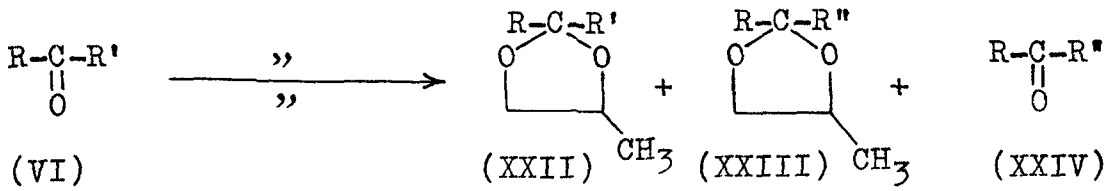
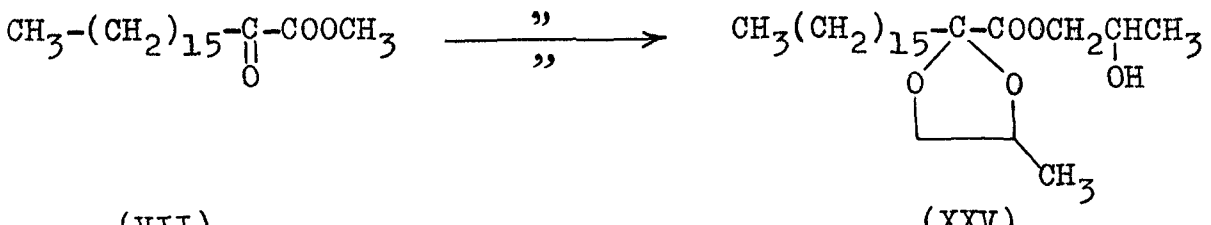


(VI) (XXII) (XXIII) (XXIV)

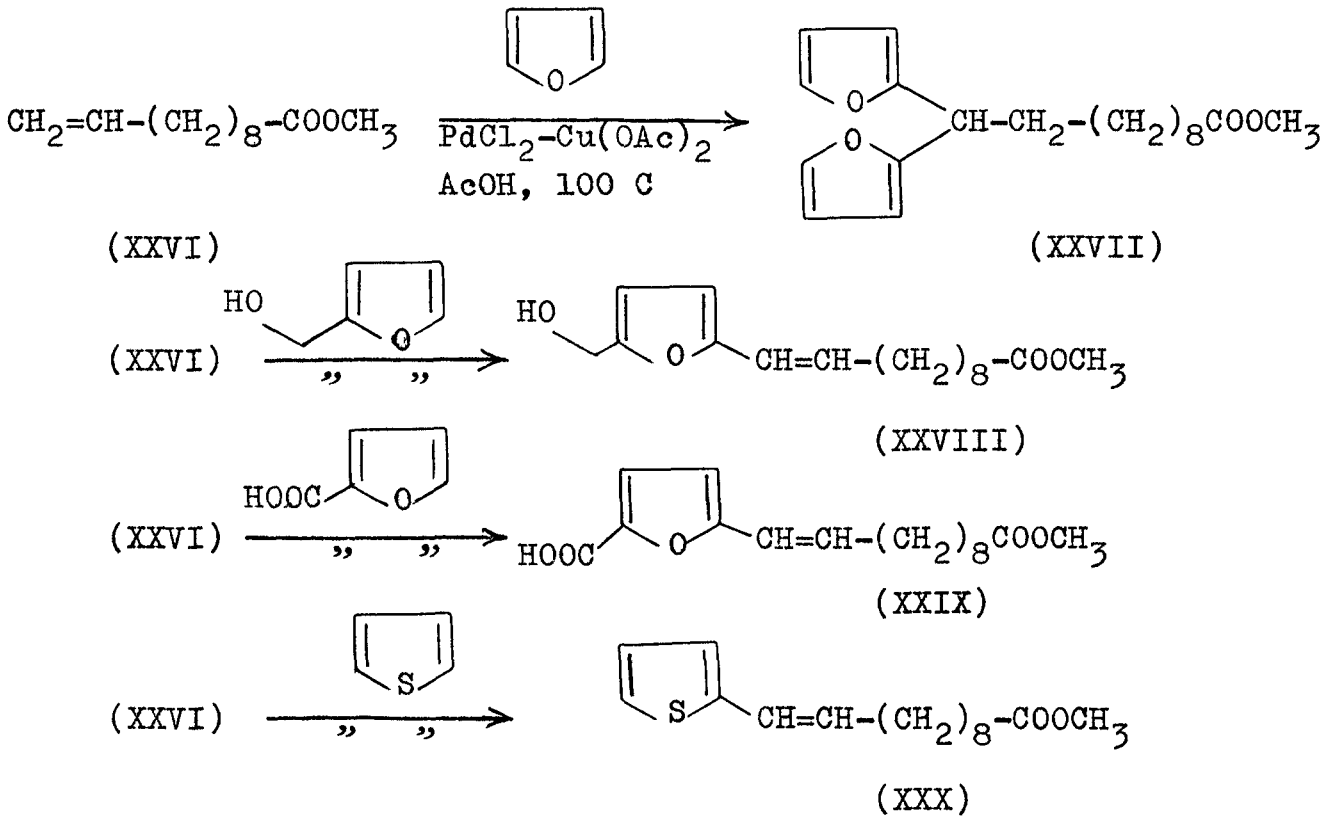
R = $CH_3(CH_2)_8$; R' = $(CH_2)_7COOCH_3$; R" = $(CH_2)_7COOCH_2CH(OH)CH_3$



(VII) (XXV)

5. Palladium Catalyzed Alkenylation of five membered Aromatic Heterocycles with Methyl 10-undecenoate

Alkenylation reaction of the terminal olefinic (methyl 10-undecenoate) ester (XXVI) was carried out with furan, furfuryl alcohol, 2-furoic acid, thiophene and pyrrole according to the procedure of Fujiwara and coworkers, using equimolar amounts of $PdCl_2$, $Cu(OAc)_2$, the heterocycles and olefinic ester in a solution of dioxan and acetic acid at 100 C. The corresponding monoalkenylated products were obtained, except with furan and pyrrole. In the case of furan an unusual product (XXVII) was obtained while the reaction did not occur when pyrrole was used.



Introduction

NINETY percent of the world production of approximately 60 million tons of animal and vegetable fats and oils is consumed in edible products. Dietary fat is more important since its calorie density is more than twice than that of proteins and carbohydrates. The fatty acids, apart from being the constituents of the cell membrane, take part in a number of fascinating reaction leading to prostaglandin, thromboxane and prostacyclines.

In India, the chronic shortage of edible oils has led to heavy imports of oilseeds from abroad. This situation has necessitated a search for the available oilseeds found abundant in the forest flora. In recent years the utilization of fatty acids as agrichemicals as a substitute to petrochemicals find their way into a variety of industrial uses and most of them mainly through derivatization.

Based on the present trends in the Research and Development program of oils and fats, it appears that future research shall have to be intensified in four directions: (a) chemical-synthesis of fatty chemicals, (b) biological-improving nutritional qualities of edible oils, (c) industrial-applications of non-edible oils for non-food uses and

(d) agricultural-agrononic research and biotechnology. It is doubtful that the present commercial oilseed crops can be expected to fulfill all the needs of the oil-based industries. The oleochemical industry has expanded dramatically during recent years. Thus derivatization of fatty acids is the main thrust area in the field of oleochemistry.

Keeping in view the current status of the availability and industrial needs of a developing country like India, an intensive investigation to explore new minor oilseeds is the only alternative to tide over the crisis of oils and fats. There is an urgent need also to utilize the minor seed oils rich in specific fatty acids for the production of fatty chemicals which could be substituted in place of the costly petrochemicals. It is with this objective that the present work has been undertaken to carry out phytochemical screening of minor oilseeds and to synthesize new heterocyclic fatty chemicals from naturally occurring fatty acids.

PART ONE

Compositional Studies of Minor Seed Oils

Theoretical

Oilseeds, next to food grains, occupy an important position in Indian agriculture. These are cultivated on about 19 million hectares of land and contribute nearly 6 per cent to the Gross National Product. Even then, there is an acute shortage of edible as well as non-edible oils and fats. Currently, 1.2-1.25 million tons of edible oils are imported at a cost of over 10,000 x 10^6 rupees. It indicates clearly that productivity does not match with increase in population.

Oils and fats are found very significant physiologically as well as chemically. The calorie density for dietary fats are also found more than twice than that of proteins and carbohydrates. Fatty acids are essential dietary requirements for their link with the prostaglandins and their involvement in cell membrane formation.

Recognizing these and other potentialities, it is high time for oil chemists and technologists to evolve various methods and many new concepts in increasing the availability of seed oils conforming with the needs of world in general

and of developing countries in particular. In this context, efforts have been directed to explore minor seed oils from neglected forest wealths of indigenous origin and ascertain their edible and non-edible uses. Exploitation of minor seed oils like mohwa, neem, kusum, karanja, sal, mango, rice bran, muskmelon and watermelon are yet to be revealed to their fullest extent. However, most of them have been well recognised in edible industries. Efforts are also being drawn up to realize full potential of industrial seed oils like castor, jajoba, Vernonia, Wrightia, Hydnocarpus etc. thereby substituting those oils which may meet food end. In this direction, we have also opted schemes of seed oil screening in our laboratory.

The naturally occurring fatty acids of vegetable origin contain even number of carbons (4-24) in a straight chain with a terminal carboxylic group, which may be fully saturated or unsaturated. About 800 fatty acids containing a variety of functional groups i.e. olefinic, acetylenic, allenic, cyclopropenoid, oxo, hydroxy, epoxy etc. have been discovered and isolated in the plant species. Many reviews[1-5] dealing with these fatty acids have been published. It has been suggested that environmental factors affect the composition of the component fatty acids of seed lipids.

It was noted that C_{16} fatty acids in seed fats are not as common as C_{18} and short or medium chain acids are rare.

Palm oil is the best source of palmitic acid. Recently, Osman et al.[6] found that Ochna squarrosa is a rich source of palmitic acid and tripalmitin. Hexadec-cis-6-enoic acid (82.2%) in Thunbergia alata[7], hexadec-cis-9-enoic (palmitoleic) acid in Zanthoxylum alatum[8] and Ochna artopurpuria[9] have been reported in fairly good amount. Recently ω-5 monoenes have been reported in the seed oil of Grevillea roubsta[10]. In our laboratory, two seed oils of Labiatae family, Leucas cephalotus[11] and L. urticifolia[12] have been reported to contain laballenic acid. Fatty acids with conjugated and non-conjugated double bonds occur in many seed oils. Recently the seed oil of Diplocyclos palmatus[13] has been found to contain octadec-cis-9, trans-11,cis-13-trienoic (punicic) acid to the extent of 38.2%. Cyclopropenoid (sterculic and malvalic) fatty acids (CPFA) generally occur in four orders[14-16] (Malvales, Sapindales, Ebnales, Rhamnales) of plant species. From the author's laboratory a number of seed oils containing varying amounts of CPFA have been reported[17-24]. Biosynthesis of cyclopropenoid acids in higher plants has been studied[25,26]. Sterculic and malvalic acids often occur together and some times may be accompanied by small amounts of their dihydro derivatives.

Natural Oxygenated Fatty Acids

Oxygenated fatty acids are considered essential intermediates in a variety of basic studies in fatty acid chemistry. Recently the oxygenated fatty acids have attracted much attention in the

industrial processes concerned with the oxidation of the drying oils. Recently the structure and biosynthesis of some natural oxygenated acids have been reviewed[27]. Among the oxygenated fatty acids, hydroxy and epoxy acids are widely distributed in plant species.

Hydroxy Fatty Acids

Formation of hydroxy acids in plants are believed to occur by the hydration of unsaturated acids[28] or directly by the oxidation of saturated carbon atom in the presence of water and molecular oxygen respectively. The only commercially available hydroxy vegetable oil is castor oil (Ricinus communis), which contains 90% ricinoleic (12-hydroxy-cis-9-octadecenoic) acid[29]. From our laboratory Siddiqui et al.[30] reported 84.3% ricinoleic acid from Hiptage benghalensis seed oil. Small amount of ricinoleic acid has also been reported in seed oils of Phyllanthus niruri[31] and Nymphaea stellata[32]. Ricinoleic acid is some timesaccompanied by their C_{20} homologue, lesquerolic acid. Recently, Plattner et al.[33] have reported the presence of lesquerolic acid (30%) with a trace of new hydroxy fatty (16-hydroxy-cis-13-docosenoic) acid. Quite recently a saturated hydroxy (9-hydroxydodecanoic) acid[34], a dihydroxy (9,14-dihydroxy-octadecanoic) acid[35], a β-hydroxyolefinic (9-hydroxyoctadec-cis-11-enoic) acid[36], a C_{24} non-vicinal 1,3-dihydroxy(11,13-dihydroxy-tetracos-trans-9-enoic) acid[37] and a γ-hydroxydienoic (8-hydroxyoctadec-cis-11,14-dienoic) acid[38] have been reported from our laboratory. A new acid, 15-hydroxyhenicosanoic

acid has been reported from Egyptian henbane[39] (a poisonous plant). In addition to conventional fatty acids, the seed oil of Securidoca longipedunculata contains acetic acid and a range of homologous hydroxydienoic acids[40]. Recently, α-kamlolenic (18-hydroxy-cis-9,trans-11,trans-13-octadecatrienoic) acid has been reported in Trewia nudiflora[41] seed oil. Previously this ω-hydroxy acid had been found only in the seed oil of Mallotus philippinensis[42]. The presence of 5,8,12-trihydroxyoctadec-trans-9-enoic acid in wheat bran has been demonstrated[43].

The hydroxyacetylenic fatty acids are also as numerous as hydroxyolefinic acids in seed oils. Miller and coworkers[44] isolated a number of oxygenated acetylenic acids (8-hydroxy-octadec-10,12-diynoic and 8-hydroxy-17-octadecen-10,12-diynoic acid) from the seed oil of Ongokea gora.

An isomer of ricinoleic (isoricinoleic/Strophanthus,9-hydroxy-cis-12-octadecenoic) acid was first reported by Gunstone in the seed oil of Strophanthus sarmentotus[45] (Apocynaceae). Ansari et al.,[46] from author's laboratory reported this acid as a major component of the fatty acids present in the oils of Wrightia tinctoria and W. tomentosa (Apocynaceae). Siddiqi et al.[47] have reported isoricinoleic acid as a richest source in W. coccinea seed oil. This hydroxy acid was also found in high amount in the seed oil of Holarrhena antidysenterica[48] (Apocynaceae).

Epoxy Fatty Acids

Fatty acids with epoxy groups occur naturally in seed oils of a considerable number (sixty) of plant species in twelve plant families. Krewson[49] and Earle[50] reviewed the literature on epoxy seed oils. Vernolic acid was the first acid of this class, and was characterized by Gunstone[51]. Recently from author's laboratory Vernonia volkameriaefolia[52] seed oil was discovered as an additional rich source of vernolic acid. Coronaric (cis-9,10-epoxyoctadec-cis-9-enoic) acid, an isomer of vernolic acid was discovered by Earle[50]. These two epoxy acids are structurally related to the linoleic acid. Saturated epoxy (cis-9,10-epoxyoctadecanoic) acid was reported in the seed oil of Tragopogon porrifolius[53] and in the spores of Lycopodium[54]. Its trans isomer was isolated by Vioque et al.[55] in the olive oil. Minor amounts of epoxy acids; cis-9,10-epoxy-trans-3, cis-12-octadecadienoic[56], cis-12,13-epoxy-cis-6, cis-9-octadecadienoic[57], cis-15,16-epoxy-cis-9, cis-12-octadecadienoic[58] have also been reported in many seed oils of Compositae family. A C_{20} homologue of vernolic named alchornic, cis-14,15-epoxy-cis-11-eicosenoic acid has been isolated by Kleiman et al.[59] in the seed oil of Alchornea cordifolia.

Some times two or more of these epoxy acids occur in the same oil. The co-occurrence of epoxy acids, cis-9,10-epoxy octadecanoic and cis-9,10-epoxy-cis-12-octadecenoic was noted by Mikolajczak and coworkers[60] in Helianthus annuus seed oil

in addition to the earlier report of Morris et al.[61]. The co-occurrence of coronaric and vernolic (4:1) acids in Xeranthemum annuus seed oil was also reported[62]. A new epoxy acid, cis-9,10-epoxyoctadec-12-ynoic acid was identified as a minor component of Helichrysum bracteatum[63] seed oil along with the previously identified coronaric acid. In our laboratory[64], a new epoxy (cis-3,4-epoxy-cis-11-octadecenoic) acid was isolated from the seed oil of V. roxburghii along with vernolic acid. Mucuna prurita[65] was also found to contain vernolic acid (4%) and its previously unidentified trans isomer (1%, cis-12,13-epoxy-trans-9-octadecenoic acid).

Recently from our laboratory the seed oils of M. pruriens[66], Hibiscus mutabilis[67], Abelmoschus moschatus[18], Acacia catechu[68], A. mallifera[69], Centratherum ritchei[70], H. esculentus[71], Kigelia pinnata[72], Cosmos sulphureus[73], Malva sylvestris[74] and Leonurus sibiricus[75] have been found to contain vernolic acid in varying amounts.

The epoxy acids in general may be regarded as derivatives of oleic, linoleic and linolenic acids, in which one of the double bond is epoxidized through metabolism.

Detection and Structure Determination of Fatty Acids

Only few years back the complexity in the analysis of fatty acids has created many problems in their detection, isolation and structure determination. This picture was changed with

the advances in the methodology for lipid analysis. The chromatographic techniques used in the analysis of oils are:thin layer chromatography (TLC), high performance liquid chromatography (HPLC), column chromatography, liquid column chromatography (LCC)[76-78], partition, adsorption, ion-exchange and complexation chromatography and gas liquid chromatography (GLC)[79]. In recent years, the preparative GLC has been employed successfully in the isolation of pure fractions from a complex mixture. HPLC is the new evolution in the chain of chromatographic techniques. Fatty acids have been separated as methyl, phenyl and 2-naphthyl esters employing HPLC[80-85]. The other valuable techniques in the analysis of lipids are: counter current distribution, droplet counter current distribution, urea and thiourea adduct separation, chemical and spectroscopic methods.

Like wise, various spectroscopic techniques, such as UV, IR, high resolution ^{1}H nuclear magnetic resonance (^{1}H NMR), ^{13}C NMR [86], liquid chromatography mass spectrometry (LCMS)[87], gas chromatography mass spectrometry (GCMS) and chemical ionization mass spectrometry (CIMS)[88] offer remarkable solutions and unexpected advantages for the analysis of unknown fatty compounds.

In practice, when the unknown fatty acid is not pure but is contaminated with other isomers, these physical methods can not alone provide the complete information about the

structure. In such cases the obvious choice is to use the chemical methods like catalytic hydrogenation, hydroxylation, oxidative degradation, partial hydrogenation, oxidation, photo-oxygenation, alkoxybromination[89], thiocyanation[90], oxyselenation[91], Diels-Alder reaction and hydrogen bromide reaction. Recently alkylthiolation reaction[92] has been used to determine the position of the double bond.

Hydroxy and Epoxy Acids

Hydroxy and epoxy acids can be detected qualitatively by direct TLC. Epoxy groups respond to picric acid[93]. Quantitative determination of epoxy fatty acids are done by HBr titration(3 C). Erythro and threo isomers of dihydroxy acids are resolved by using silica gel impregnated with silver nitrate[94] or boric acid[95].

Adsorption column chromatography has been very effective for separating saturated and unsaturated hydroxy fatty acids. The complexation chromatography separates the hydroxylated lipids according to number, position and configuration of hydroxyl groups on borate-impregnated adsorbents. GLC is a very powerful tool for the detection and estimation of hydroxy and epoxy fatty acids. The hydroxyl group can be masked by methyl iodide and silver nitrate acetylation, trimethyl-silylation (TMS) or trifluoroacetylation[96]. The position of epoxy and hydroxy groups in chain can be fixed by GLC

analysis provided that authentic samples are available. GLC behavior of cis and trans-epoxy esters is summarized by Gunstone and coworker[97].

HPLC in both analytical and preparative modes has been usefully employed in the separation of hydroxy fatty acids[98,99]. It has been used to separate E and Z isomers prior to their further examination by capillary gas chromatography[100]. This form of chromatography has also been applied to glyceride analysis. Separation is influenced by chain length and by unsaturation and provides more information than most of the gas chromatographic procedures[101]. Better results have been claimed with reversed phase system[102] and the use of silver ion to enhance separation has been reported[103]. Claims have also been made for the advantageous use of 1-chloromethylisation[104], 9,10-diaminophenanthrene[105] and 9-diazomethylanthracene[106] for derivatization of fatty acids for HPLC.

IR, NMR and mass spectral techniques are very much helpful in ascertaining the structure of hydroxy and epoxy acids present in the oil. The extensive application of wide-line NMR in the oils and fats industry has been reviewed[27]. Reviews have also been published on mass spectrometry[107], its uses in the location of double bonds[108], oxygenated functions and on derivatives suitable for mass spectrometry[109] in lipid analysis. N-Acylpyrrolidides have certain advantages over esters for mass spectrometry[52]. Tulloch[110] has reported MS studies of a range of hydroxy- and oxo-hexadecanoates. CIMS has also been applied to the detection of hydroxy fatty acids[111].

Discussion

Chapter 1

Minor Seed Oils

As a matter of fact, the chemical screening of seed oils continues to reveal nature's diversity. Recently, Osman and Fasih[5] have published a survey of potential oilseed species of forest origin. The review has indicated a few oil-rich species that show sufficient promise as alternative source of vegetable oils. Till now, the species from less or rare families have received only limited study. However, some of these little known species seem to provide excellent candidates for the production of desirable seed oils. In continuation of 'Minor Seed Oil Screening' program carried out in our laboratory[112], a study of five seed oils from species of five different plant families was undertaken.

The quantitative estimation of fatty acid components on a gas chromatogram was achieved by comparing retention times with those of lipid standards. The results of quantitative, direct argentation and reversed phase TLC supported the findings of GLC analysis. Unusual functionality

including *trans* unsaturation and conjugation were checked by IR and UV spectroscopy respectively. The absence of unusual functions were confirmed by various chromatographic and spectroscopic techniques. The seed and oil chracteristics are shown in Table 1 along with the GLC analysis of the methyl esters of the oils.

Tephrosia villosa, Pers. (item 1), of Leguminosae, is a shrub, found throughout India to Ceylon, Mauritius and Tropical Africa. Its leaves are used in dropsy[113]. It had the ordinary palmitic-oleic-linoleic type of composition. Such type of composition has earlier been reported in many *Tephrosia* species[114] and it has been well documented that leguminosae seed fats resemble this type of composition. Among unsaturated acids, the GLC analysis showed linoleic acid as the major component (44.2%) followed by oleic acid (18.2%). The total saturated acids (12:0, 0.9; 16:0, 25.6 and 20:0, 5.1%) are 31.6%. Thus this oil may be classified as linoleic-rich seed oil.

Bassia species (item 2, Sapotaceae) are usually trees. The fatty acid composition reported here agreed with the previous report[115] on the pattern of the composition of Sapotaceae seed oils (18:1 > 18:2 > 16:0 > 18:0). Recently some species of this family have been reported[4] to contain cyclopropenoid fatty acids.

Table 1

Analytical Data on Seeds and Oils

Species (Family)	Oil Content %	Oil Properties			Methyl Ester Composition % by GLC				
		IV[a]	SV[b]	RI[c] (n_D^{30})	16:0	18:0	18:1	18:2	18:3
1. *Tephrosia villosa* (Leguminosae)	3.9	115.8	193.2	1.4861	25.6	trace	18.2	44.2	5.7
2. *Bassia* species (Sapotaceae)	6.0	101.2	190.4	1.4824	16.0	6.5	46.5	28.9	0.4
3. *Polygonum* species (Polygonaceae)	4.2	123.6	197.8	1.4724	41.2	trace	4.8	8.5	37.8
4. *Hydrolea zeylanica* (Hydrophyllaceae)	14.1	145.4	195.2	1.4961	11.4	4.9	32.8	20.9	28.2
5. *Lycium barbarum* (Solanaceae)	18.0	87.1	192.3	1.4621	38.8	1.8	27.9	27.4	1.4

Others: Item: 1. 12:0, 0.9; 20:0, 5.1%
2. 14:0, 0.5; 20:0, 0.4; 22:0, 0.6%
3. 14:0, 7.3%
4. 12:0, trace; 14:0, trace; 20:0, trace
5. 14:0, 0.3; 20:0, 1.9%

a = Iodine Value, b = Saponification Value, c = Refractive Index.

The oil is composed of oleic (46.5%), linoleic (28.9%) and linolenic (0.4%) acids as unsaturated components. The combined content of oleic and linoleic acids (75.4%) indicated that this oil belongs to the category of 'semi-drying oils'. Among the saturated acids, palmitic acid was found as a major component. The oil also showed the presence of eicosenoic and docosenoic acids in trace amounts.

Polygonum species (item 3, Polygonaceae) is a herb and occurs mainly in upper gangetic plain, himalayan and the north-west frontier regions. Previous analysis[116] of the seed oil of this family identified oleic, linoleic and palmitic as its major components. The present analysis by GLC showed a different fatty acid profile. This oil is composed of linolenic (37.8%), linoleic (8.5%), oleic (4.8%) and a high content of palmitic acid (41.2%) together with appreciable amount of myristic acid (7.3%). The presence of myristic acid is not much common in this family.

Hydrolea zeylanica, Vahl. (item 4), of the family Hydrophyllaceae is found throughout India in wet places and often grow in rice fields. They possess some antiseptic properties[113]. A scanning of literature revealed no report on fatty acid composition of any species of the genus Hydrolea. Our GLC analysis indicated 81.9% total unsaturated acids. The combined content of oleic (32.8%), linoleic (20.9%) and linolenic (28.2%) acids, the characteristic of 'vegetable

drying oils', was a special feature of this less familier indigenous seed oil.

Lycium barbarum, Linn. (item 5, Solanaceae), is a spinous shrub. Its young leaves contain hydrogen cyanide[113]. Solanaceae seed oils were known to be rich in linoleic acid. The present sample of L. barbarum contains 27.4% of linoleic acid out of total 56.7% of unsaturated acids. This species falls in the category of oleic-linoleic rich (56.7%) oils. However, the high concentration of palmitic acid (38.8%) limits its application as 'semi-drying oil'. The other saturated acids in minor amount are myristic (0.3%), stearic (1.8%) and eicosenoic (1.9%).

In general the seed oil compositional data indicated that the oils of Bassia sp. and T. villosa were characterized by the presence of 75.8-68.1% unsaturated acids, a good characteristic of edible oil. The oil of Bassia sp. was extremely rich (~76%) in combined oleic-linoleic acid content and somewhat resembled sunflower seed oil. The low oil yields preclude its use as a source of minor oilseeds. Further, it must be assumed in a screening program that the sample analyzed is representative to serve as a guide for further study of oils for specific uses and for evaluation as a prospective crop.

Chapter 2

Hydroxy Acid in Strychnos potatorum Seed Oil

Strychnos potatorum, Linn. (Loganiaceae), is a tree and belongs to Bengal and found plentiful in southern India and Burma. Seeds are non-poisonous and used in diarrhoea, diabetes and given in irritation of urinary organs[113]. Previous work[117] on Strychnos seed fats revealed low percentage of saturated acids and higher percentage of oleic and non-conjugated diene. S. potatorum has earlier been analyzed only for its oil (2.8%) and protein content[118].

Present work on S. potatorum seed showed that its oil content is 8%, which contains a monohydroxy acid (24.90%). The monohydroxy acid was isolated from the total mixed fatty acids (MFA) by preparative TLC and characterized as 9-hydroxy-cis-12-octadecenoic (isoricinoleic) acid. Oil and seed characteristics were determined according to AOCS methods[119] and results are summarized in Table II. The iodine value (I.V.) of the oil was found somewhat higher than the theoretical value. This observation is consistent with the literature[45] that the hydroxy fatty acid containg seed oils give higher I.V. apparently because of the involvement of the reagent with the hydroxy group.

Table II

Strychnos potatorum Seed and Oil

Oil Content of Seeds, %	8.0
Iodine Value	85.4
Saponification Value	189.5
Refractive Index n_D^{30}	1.4836

Table III

Fatty Acid Composition of *S. potatorum*

Component	Area % by GLC
Palmitate	25.2
Stearate	2.9
Oleate	28.9
Linoleate	15.4
Linolenate	2.5
Isoricinoleate	24.9

IR and UV spectral analysis ruled out the presence of trans unsaturation and conjugation in the oil. In IR spectrum a strong band at 3400 cm^{-1} confirmed the presence of hydroxyl function. Direct TLC of the methyl ester showed a spot little lower than the methyl ricinoleate, and similar to methyl isoricinoleate. Argentation TLC of the mixed methyl ester showed a spot similar to that of an authentic isoricinoleate. Spots for saturated, monoene, diene and triene were also observed.

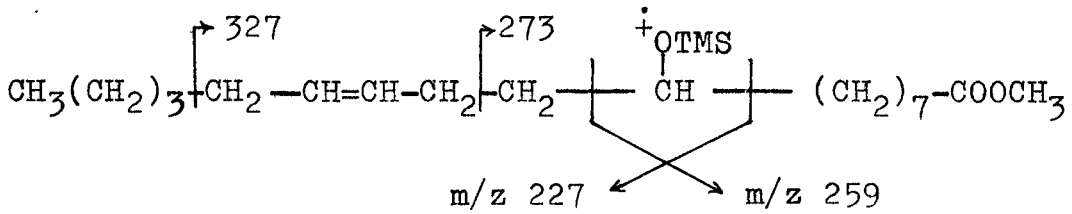
Quantitation of component acids was made by GLC separation of the methyl ester as their trimethylsilyl (TMS) derivative on a polar column (DEGS, 15%). The weight percentages of the component esters were calculated from the area of the recorded peaks and showed in Table III.

For the identity of this hydroxy acid, a pure acid sample was obtained by preparative TLC of MFA of the seed oil. The IR of the pure hydroxy fraction showed bands at 3400(hydroxy), 1710 (acid carbonyl) and 1640 cm^{-1} weak (unsaturation). This IR spectrum was found identical to that of an authentic sample of isoricinoleic (9-hydroxy-cis-12-octadecenoic) acid isolated from Wrightia tinctoria seed oil[46]. Its methyl ester's NMR spectrum exhibited characteristic signals besides the usual fatty chain signals. These signals appeared at δ 2.15 m (6H, methylene protons α-to ester carbonyl and

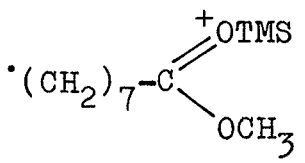
unsaturation), 3.3 m (1H, -C<u>H</u>-OH), 5.25 m (2H, -C<u>H</u>=C<u>H</u>-), 2.35 m (1H, -CH-O<u>H</u>, D_2O exchangeable). After acetylation of hydroxy acid, the IR spectrum was deprived of hydroxy absorption and the acetate bands appeared at 1730 and 1210 cm^{-1}. Its NMR spectrum exhibited no unusual features apart from two signals at δ 2.1 s (3H, -OCOC<u>H</u>$_3$) and 4.7 m (1H, -C<u>H</u>-OCOCH$_3$).

The catalytic total hydrogenation (Pd-C) of the hydroxyolefinic acid gave a saturated 9-hydroxyoctadecanoic acid melting at 76 C (lit. mp. 75 C)[120].

The structure of hydroxy acid (I) was further supported by MS (Fig. 1) studies of the TMS derivative of the hydroxyolefinic ester. It showed small molecular ion peak at m/z 384. Structure-revealing ions were observed at m/z 259 and 227 and



M^+ 384



m/z 230

a TMS rearrangement ion at 230. The ion peaks at 227,

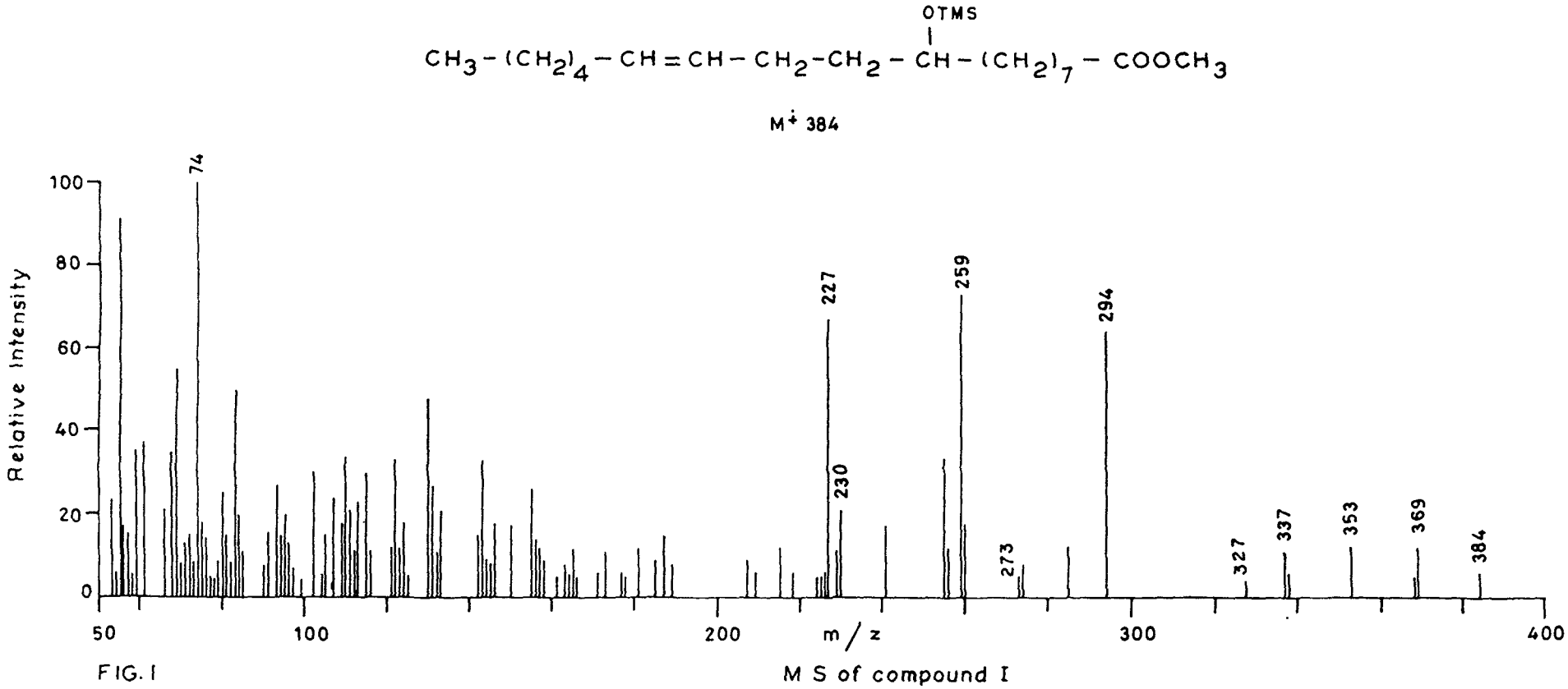


FIG. I

M S of compound I

259, 273 and 327 confirmed the position of hydroxy group at C9 and double bond at C12. As reported[121] earlier these fragment ions of about equal intensity are characteristic and observed when TMS and double bond are separated by two methylene groups. The fragment ions at 369 (M-15), 353 (M-31), 337 (M-47), 294 (M-90) and other lower mass ions were also observed. Thus the hydroxy acid isolated from S. potatorum was characterized as 9-hydroxy-cis-12-octadecenoic acid.

The seed oils of few species of Loganiaceae have been studied[117] and it has been observed that usual fatty acids occur in this family. A large number of saturated, olefinic and acetylenic hydroxy fatty acids have been reported in a broad spectrum of plant families. But the occurrence of isoricinoleic acid has generally been noted in the seed glycerides of the Apocynaceae [45-48]. The present work on S. potatorum describes the presence of isoricinoleic acid (24.9%) for the first time in this family.

Chapter 3

Epoxy Acids in Siegesbeckia orientalis Seed Oil

Siegesbeckia orientalis, Linn., S. brachiata (Compositae) is a common plant found throughout India and China. Antiseptic properties have been ascribed to the fresh plant. It is strongly recommended in the diseases of urethra, syphilis and have good effect in ringworm and some other parasitic eruptions[113].

The oil was extracted from the ground seeds of S. orientalis with petroleum ether (bp. 40-60 C). The analytical values for seeds and oil were determined according to the procedures recommended by AOCS methods[119] and the data were summarized in Table IV. The oil responded to picric test[93] indicating the presence of epoxy acid. The UV spectrum of the oil showed no conjugation. The oil was titrated with HBr according to the procedure of Harris et al.[122] at 3 C and 55 C and the results were expressed as hydrogen bromide equivalent (HBE). Titration results indicated that the oil contained 19.2% of HBr reactive epoxy acids. The other HBr reactive acids were not detected by Halphen test[123] and IR spectrum. The oxygenated and non-oxygenated fractions of the total methyl ester after transesterification, were separated by preparative TLC.

Table IV

Siegesbeckia orientalis Seed and Oil

Oil Content of Seeds, %	18.2
Iodine Value	94.2
Saponification Value	194.3
Refractive Index, n_D^{30}	1.5024

Table V

Fatty Acid Composition of *S. orientalis*

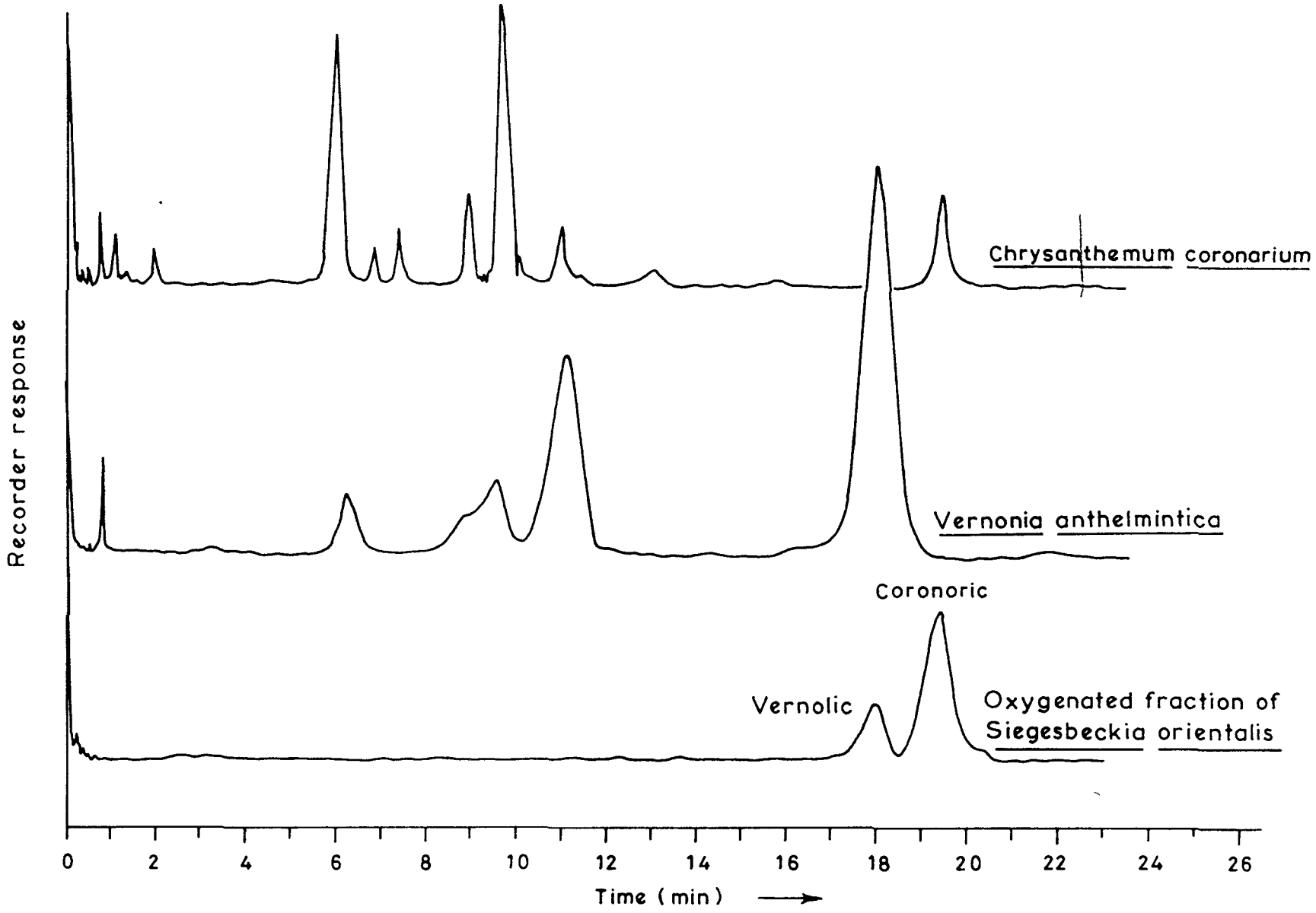
Component	Area % by GLC
Myristate	16.4
Palmitate	15.3
Stearate	4.7
Oleate	7.3
Linoleate	35.6
Linolenate	0.6
Vernolate	4.0
Coronarate	16.0

Quantitative estimation of fatty acids was carried out by GLC analysis of the total methyl ester. GLC data (Table V) regarding epoxy acids agreed fairly well with that obtained by HBr titration.

The non-oxygenated fraction responded no Halphen test[123] indicating the absence of cyclopropene acids. The UV and IR spectra showed no conjugation or any unusual functionality including *trans* unsaturation.

Characterization of the Oxygenated Fraction

This fraction responded to picric acid TLC revealing the presence of epoxy function. Its IR spectrum showed a weak band at 840 cm^{-1}, a characteristic absorption of *cis* epoxides. Its NMR spectrum exhibited signals at δ 5.4 m (2H, $-C\underline{H}=C\underline{H}-$), 3.6 s (3H, $-COOC\underline{H}_3$), 2.72 m (2H, $-C\underline{H}\!\!-\!\!\!\diagup\!\!\diagdown O\diagup\!\!\diagdown\!\!-C\underline{H}-$), 2.18 m (6H, $-C\underline{H}\!\!-\!\!\!\diagup\!\!\diagdown O\diagup\!\!\diagdown\!\!-CH-C\underline{H}_2-CH=CH-C\underline{H}_2-$ and $-C\underline{H}_2-COOCH_3$), 1.35 br s (chain $-C\underline{H}_2-$) and 0.9 t (terminal $-C\underline{H}_3$). The possibility for the occurrence of oxygenated acids other than epoxy acids in the oil was ruled out on the basis of IR, UV and TLC. The TLC of this fraction was not homogeneous and the major component of this fraction has R_f slightly lower than that of methyl vernolate, and corresponded to methyl coronarate[60]. The GLC chromatogram (GLC 1) of the esters of oxygenated fraction clearly showed two peaks corresponding to the authentic sample of methyl vernolate and methyl coronarate isolated from *V. anthelmintica*

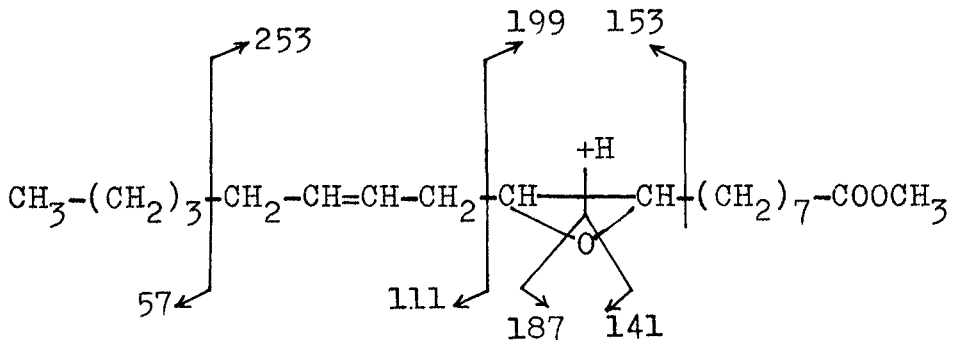


GLC.1 GLC Chromatograms of Methyl Esters

and C. coronarium seed oil respectively. By GLC analysis this fraction was identified as a mixture of methyl vernolate (20%) and methyl coronarate (80%).

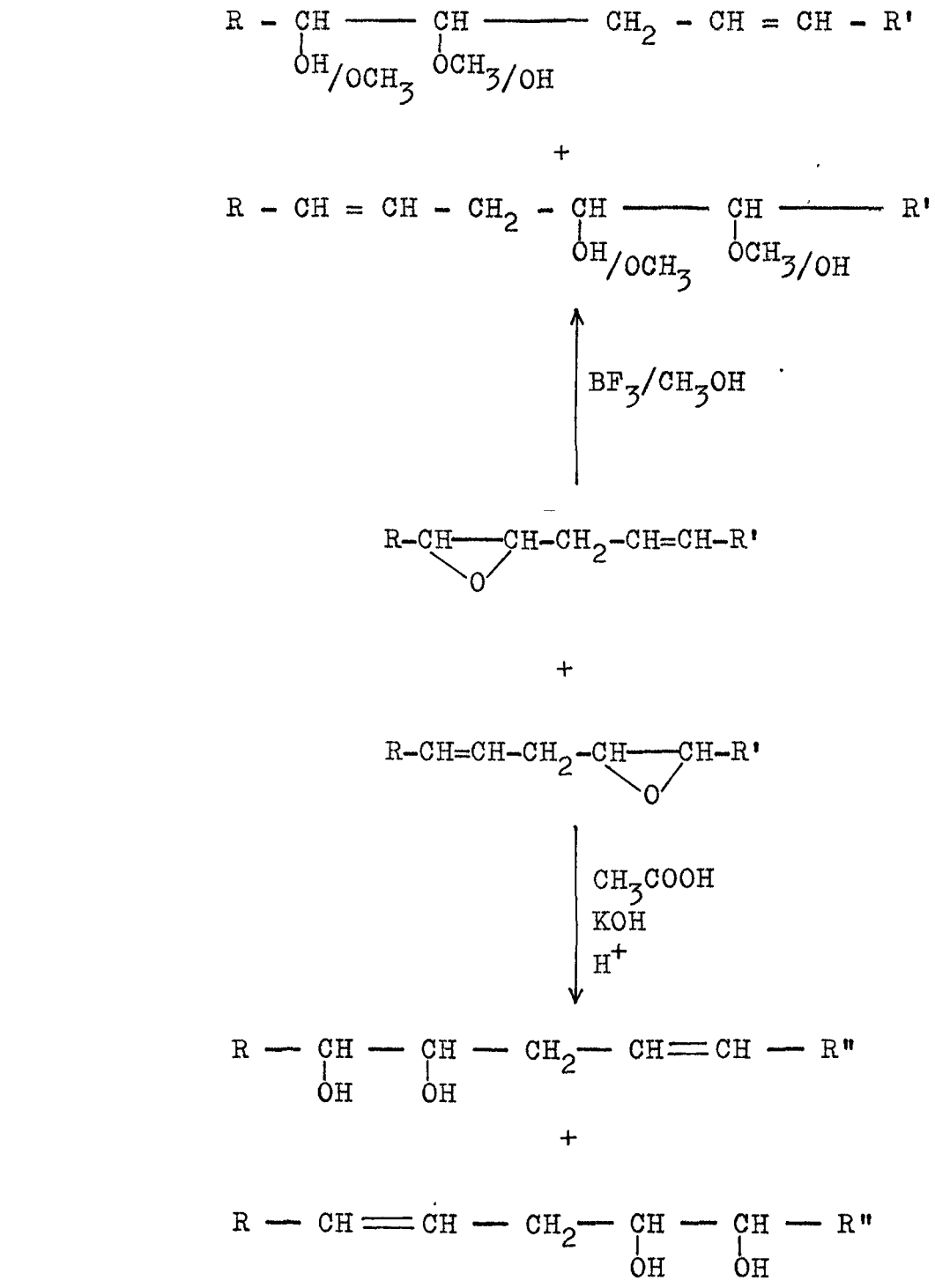
Characterization of epoxy acids was performed by direct acetolysis of the oxygenated fraction (40 mg) followed by saponification and acidification according to Gunstone's procedure[51] (Scheme 1). The resulting dihydroxy acids had the melting point 58-59 C. The melting point of this hydroxy acid mixture (58-59 C) was closely reproduced by using a mixture of known dihydroxy derivatives of coronaric (mp. 60-60.5 C) and vernolic (mp. 49-50 C) acids in the same proportions (4:1).

The mixture of the coronaric and vernolic acids was further confirmed by the study of mass spectrometry. The mass spectrum of the methyl esters of epoxy acids (Fig. 2) showed the molecular ion peak at m/z 310 along with important peaks at 292 ($M-H_2O$), 279 ($M-OCH_3$), 250 ($M-C_2H_4O_2$), 239, 113, 227, 101, 199, 153, 197, 111, 167, 253, 187, 141 with other low mass ions. The genesis of these fragment ions are given below.



Methyl coronarate (M^+ 310)

Scheme 1



R = CH_3-$(CH_2)_4$; R' = $(CH_2)_7$-$COOCH_3$; R" = $(CH_2)_7COOH$

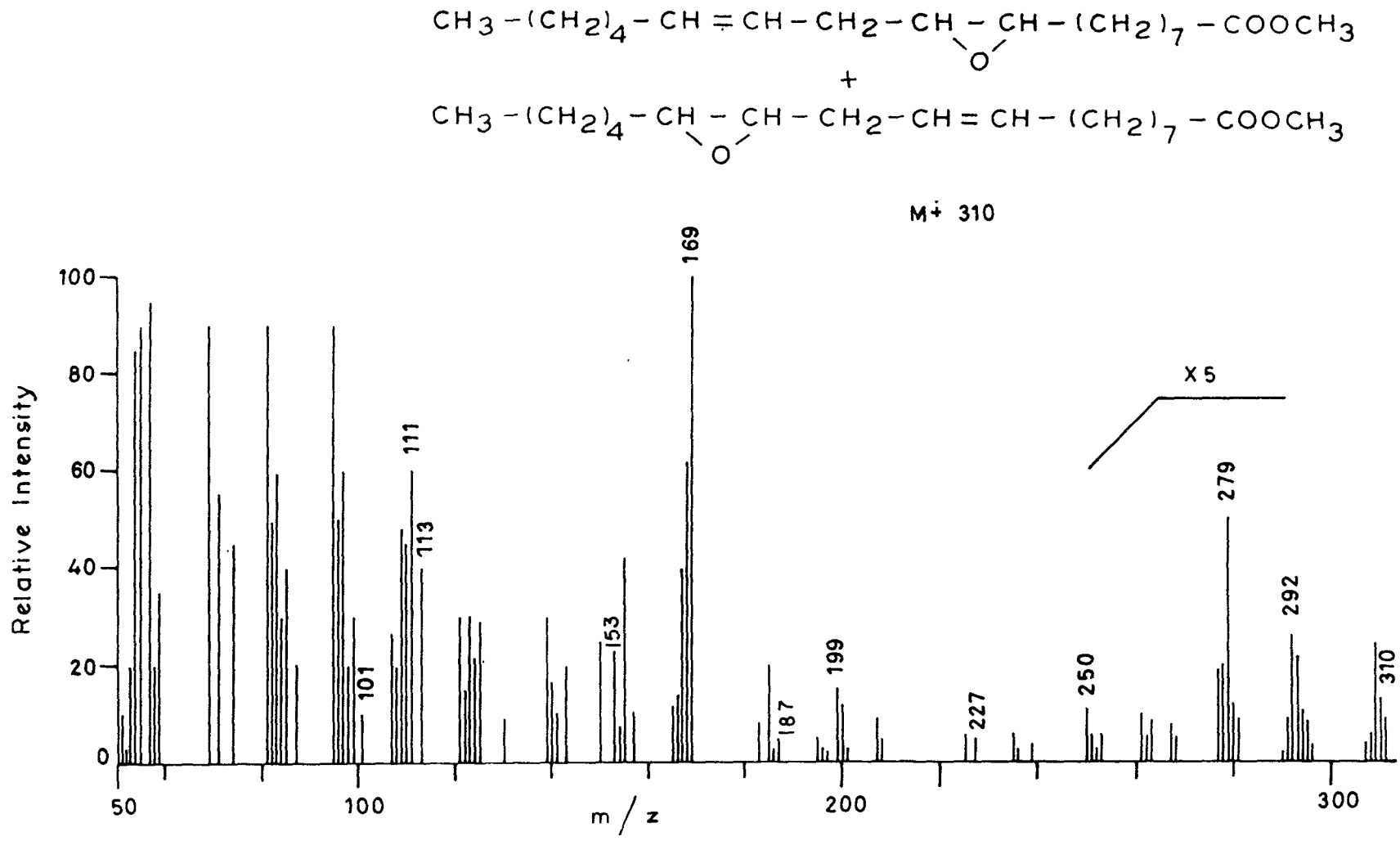
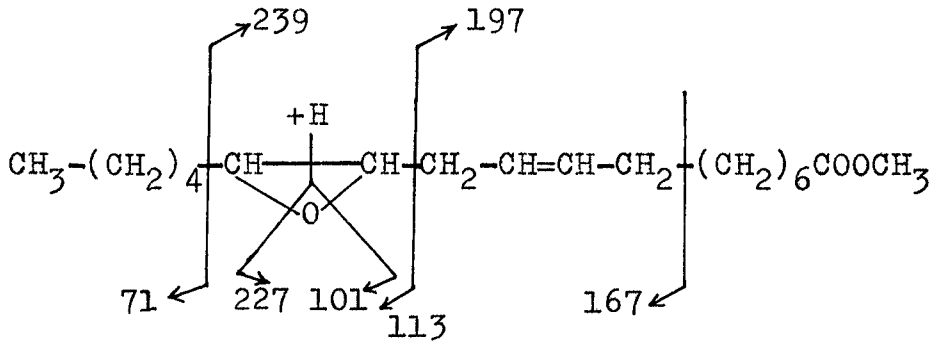


FIG. 2 M S of oxygenated fraction (methylester of Epoxy acids)



Methyl vernolate (M^{+} 310)

The above mentioned fragment ions showed that the epoxy component was the mixture of coronaric and vernolic acids. The α-cleavage fragments at 199 and 113 containing epoxide groups are more abundant than α-cleavages at 239 and 153 on other side of epoxy functions. This difference in the intensity showed that the epoxy group is separated by allylic double bond[121].

This observation was further confirmed by the mass spectrum of methoxy-hydroxy derivative of the epoxy ester (Fig. 3). It showed no molecular ion peak. The parent ion observed at m/z 324 ($M-H_2O$) along with other significant peaks at 292 ($324-CH_3OH$), 279 [$M-(CH_3OH+OCH_3)$], 285, 271, 241, 231, 227, 201, 199, 197, 187, 186, 155, 145, 142, 115, 111, and 101. The formation of these ions can be given according to following schemes.

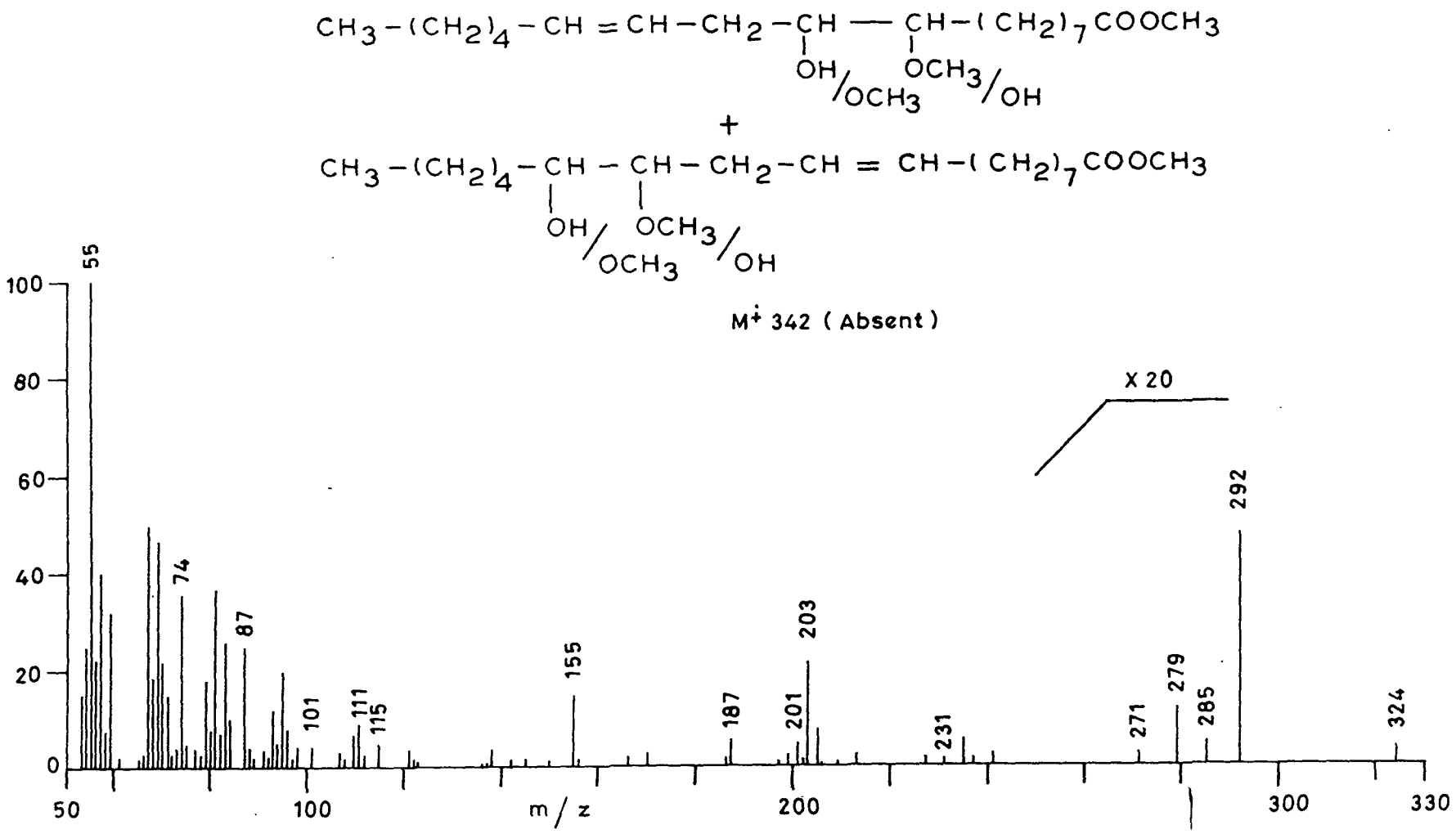
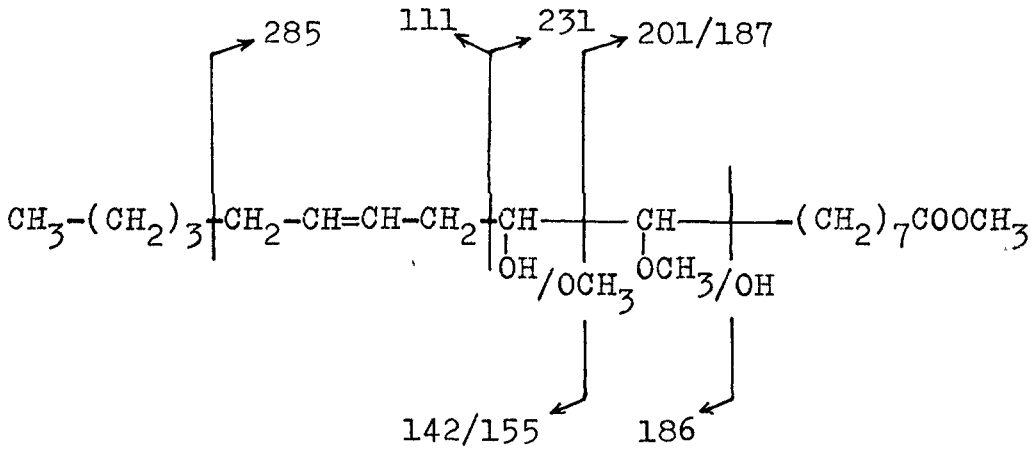
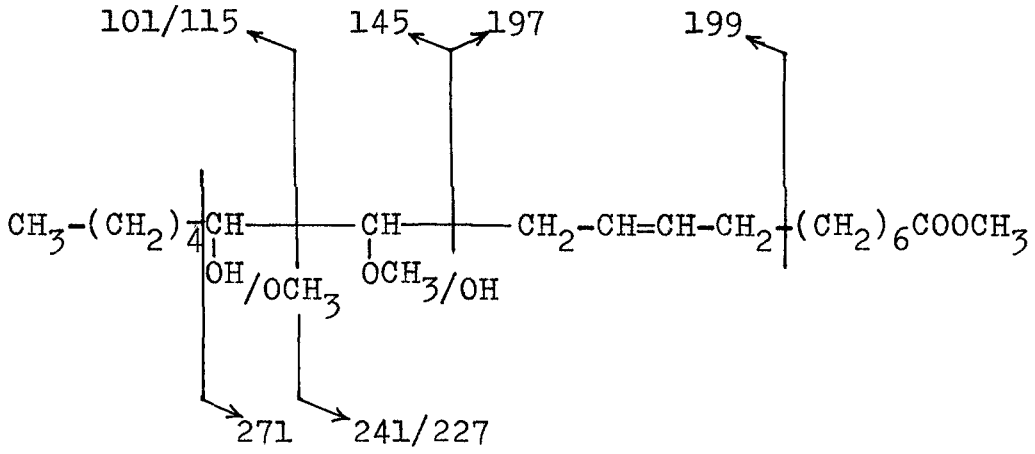


FIG. 3 M S of methoxy hydroxy derivative of epoxy ester





M^{+}342 (absent)

The other salient and lower mass ion peaks were observed at 237 [285-(OH+OCH_3)], 235 (237-2H), 213 (231-H_2O), 205 (237-CH_3OH), 203 (235-CH_3OH), 170 (201-CH_3O), 138 (170-CH_3OH) 87 (115-28), 84 (115-31), 83 (101-H_2O or 115-32), 74 (McLafferty) and 55 (base peak).

On the basis of above chromatographic and spectroscopic results it was confirmed that the oxygenated fraction was a mixture of coronaric and vernolic acids.

Previous work[56-58] on the seed oils of Compositae family revealed the presence of epoxy acids as the minor or major constituents of their glycerides. Although only one epoxy acid is found in most of the oils, in others two or more are present. The coronaric acid co-occurs with 9,10-epoxystearic acid in the different varieties of sunflower seed oils[60]. GLC analysis of S. orientalis seed oil indicated the presence of 20% epoxy acids (4% vernolic and 16% coronaric). The co-occurrence of these two epoxy acids in about the same proportion (2% and 8%) was previously reported in Xeranthemum annuum[62] seed oil of Compositae.

Experimental

All melting points were taken on Kofler apparatus and are uncorrected. Infrared (IR) spectra (expressed in cm^{-1}) were obtained on Pye Unicam SP 3-100 spectrophotometer, usually as nujol mulls, neat, solution ($CCl_4/CHCl_3$) or thin films on KBr discs. Ultraviolet (UV) spectra of oils were recorded on DK-2 spectrophotometer in methanol. Nuclear magnetic resonance (NMR) spectra were recorded at 60 MHz on a Varian A60 spectrometer, using 10-15% solution in CCl_4 or $CDCl_3$ with tetramethylsilane (TMS) as internal standard. All chemical shifts are given in ppm downfield from TMS (δ=0). The abbreviations " s,d,m,br and t" denote "singlet, doublet, multiplet, broad and triplet" respectively. Mass spectra were measured with JEOL JMS-D300 mass spectrometer at 70 eV. All the mass fragmentation schemes are to be considered tentative in the absence of accurate mass measurement.

Thin layer chromatography (TLC) was performed on glass plates with 0.25 mm or 1.00 mm thick layer of silica gel or 20% silver nitrate impregnated silica gel with 20% or 30%

diethyl ether in hexane as developing solvent. The plates were visualized by spraying 20% aqueous solution of perchloric acid and heating at 110 C. Preparative plates were sprayed with 0.2% ethanolic solution of 2',7'-dichlorofluoroscein and viewed under UV light. For reversed phase TLC, the dried plates coated with silica gel were impregnated with silicon oil (0.5%). Acetonitrile/acetic acid/water (70/10/20; v/v) were used as developing solvent.

Preparation of Methyl Esters

The seed samples were collected by staff botanists from wild herbaceous plants or by purchase from commercial seed suppliers. The oils were extracted repeatedly with petroleum ether (bp. 40-60 C) in a soxhlet apparatus. The analytical values of seeds and oils were determined according to the AOCS methods[119].

Seed oils were refluxed with ethanolic potassium hydroxide. The unsaponifiable material was removed by diethyl ether extraction and the free fatty acids were obtained by acidification with dil. H_2SO_4 of aqueous layer followed by extraction with diethyl ether.

Methyl esters were prepared by refluxing the mixed fatty acids (MFA) for 1 hr in excess of methanol containing catalytic amount of sulfuric acid. In each case, the resulting mixture was diluted to the cloud point with water chilled in ice bath,

and then extracted repeatedly with diethyl ether. Combined extracts were washed with 5% aqueous sodium bicarbonate, water and dried (Na_2SO_4).

Gas Liquid Chromatography

The quantitative examination of methyl esters were carried out by using a Perkin Elmer Model-154 vapor fractometer equipped with a thermal conductivity detector, using stainless steel packed column (2 m x 3 mm) coated with 15% diethyleneglycol succinate (DEGS) on chromosorb W, 45-60 mesh. The separations were carried out isothermally at 200 C, chart speed 0.76 m/hr with hydrogen flow of 70 ml/min. Linseed, ground nut, Wrightia tinctoria, Vernonia anthelmintica and Chrysanthemum coronarium oil methyl esters were used as standards. For internal standardization, pure samples of fatty acid methyl esters (Sigma Company, USA) were used.

Isolation of Hydroxy Acid (I) from S. potatorum Seed Oil

Hydroxy acid (I) was isolated from MFA of S. potatorum seed oil by preparative TLC, using the solvent system hexane/diethyl ether/acetic acid (80/20/1; v/v). The isolated hydroxy acid (23.6%) showed a single spot on the analytical TLC plate.

(I): Analysis- (Found: C, 72.35; H, 11.45. $C_{18}H_{34}O_3$ requires: C, 72.4; H, 11.48%; IR (Neat): 3400 (OH), 1710 (COOH), 1640 weak (C=C).

The methyl ester (Ib) of this hydroxy acid was prepared as described earlier.

(Ib): NMR ($CDCl_3$): 5.25 m (2H), 3.6 s (3H), 3.3 m (1H), 2.35 m (1H, D_2O exchangeable), 2.15 m (6H, 1.3 br s (Chain-$C\underline{H}_2$-) and 0.9 (3H).

Hydrogenation of Hydroxy Acid (I)

The pure hydroxy acid (I, 0.2 g) was hydrogenated over palladium-carbon (10%) in ethyl acetate (2 ml), 45 psi at room temperature. Total hydrogenation of the acid for 12 hr gave a solid product which on crystallization from benzene yielded pure saturated hydroxy acid (II), mp. 76 C (lit. mp. 75 C)[120].

Derivatization of Hydroxy Acid (I)

(a) Acetyl Derivative: 50 mg of I was dissolved in acetic anhydride in pyridine (2 ml; 5/1, v/v) and left at room temperature overnight. The reagents were removed in a stream of nitrogen with gentle warming.

(b) Silylation of Methyl Ester (Ib): To the methyl ester (100 mg) pyridine (10 ml), hexamethyldisilazan (3.0 ml) and trimethylchlorosilane (1.0 ml) were added. The mixture was shaken for 30 sec. and allowed to stand for 3 min., then hexane (25 ml) and water (25 ml) were added. The hexane layer was removed and aqueous layer washed twice with 15 ml portions of hexane. The combined hexane extracts were washed

and dried. Then the solvent was removed in a stream of nitrogen till the odor of pyridine disappeared.

MS : M^{+} m/z 384.

Epoxy Acids from Siegesbeckia orientalis Seed Oil

Picric Acid TLC[93]: Picric acid TLC was carried out using silica gel G plate. The developing solvent was petroleum ether/diethyl ether/ acetic acid (75/25/1, v/v). The developed plate was sprayed thoroughly with 0.5 M picric acid in 95% ethanol and immediately placed in a jar saturated with the vapor of diethyl ether/ethanol/acetic acid (80/20/1, v/v). After 30 min. the plate was exposed to ammonia fumes for 1-2 min. The orange spot on a yellow background indicated the presence of epoxy group.

Hydrogen Bromide Titration[122]: The titration of weighed amount of oil with 0.1 N hydrogen bromide using crystal violet as indicator at 3 C to bluish green end point that persisted for 30 sec., furnished the selective quantitation of the epoxy fatty acids in the sample. Cyclopropenes and/or α-hydroxy-dienes react with HBr at higher temperature 55 C. The percentage of epoxy content was calculated by the equation.

$$\% \text{ epoxy} = \frac{29.45 \times N \times V}{\text{weight of the sample}}$$

where N = Normality, V = Volume of HBr consumed in titration.

Isolation and Characterization of Epoxy Acids

The methyl esters of S. orientalis, V. anthelmintica and C. coronarium seed oils were prepared by transesterification with sodium methoxide (0.5%; 10 ml/g of oil).

The total methyl ester (4.0 g) of S. orientalis was separated into non-oxygenated (3.0 g) and oxygenated (76 mg) fractions by preparative TLC, using silica gel G.

(Oxygenated Fraction) Analysis: IR (Neat): 1735 ($\underline{COO}CH_3$), 1640 weak (C=C), 840 (cis epoxide); NMR ($CHCl_3$) 5.4 m (2H), 3.6 s (3H), 2.72 m (2H), 2.18 m (6H), 1.35 br s (chain-$C\underline{H}_2$-) and 0.9 t (3H); MS : M^+ m/z 310.

Acetolysis

Oxygenated fraction (40 mg) was refluxed with glacial acetic acid (1.5 ml) for 5 hr. The mixture was then saponified, acidified and diluted with water. and extracted repeatedly with diethyl ether. After removal of solvent and crystallization from acetone and petroleum ether (3:1, v/v) the solid product, unsaturated dihydroxy acids. mp. 58-59 C, was obtained.

The unsaturated dihydroxy derivatives of vernolic and coronaric acids were obtained by the direct acetolysis of V. anthelmintica and C. coronarium seed oils as described above.

Methoxy Hydroxy Derivative[124]

The methyl ester of the mixture of epoxy acids was refluxed with BF_3-methanol (0.5 ml) for about 15 min. The reaction mixture on usual work up gave (18 mg) methoxy-hydroxy derivative of the epoxy acid esters.

MS : M^+ m/z 342 (absent). Parent ion peak at 342 ($M-H_2O$).

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PART TWO

Oxygen and Sulfur Containing Fatty Heterocycles

The functionality of fatty acid molecules and their derivatives accounts for the utility of these materials in a large variety of applications. The increasing cost of petrochemicals has diverted the attention of chemists towards the synthesis of oleochemicals from natural fats and oils and their fatty acid derivatives. These fatty derivatives are becoming essential to a variety of industries such as coatings, surfactants, plasticizers, lubricants, additives, cosmetics, perfumes, pharmaceuticals, pesticides, insecticides and polymers. In nature, heterocyclic compounds as alkaloids, vitamins and pigments are well known. But heterocyclic rings in fatty compounds are rare in nature. These heterocycles are physiologically active and control many biochemical processes of various systems and their search acted as a powerful stimulus to the further development of the chemistry of heterocyclic compounds.

Chapter 4

Derivatization of Keto Fatty Acids

Theoretical

Naturally occurring oxo (keto) fatty acids are rare. A number of synthetic keto acids are known. Since the keto fatty acids possess the $-CH_2-\overset{\overset{O}{\|}}{C}-$ group, they are capable of undergoing enolization with the formation of enol group $-CH=\overset{\overset{OH}{|}}{C}H-$, which undergoes many chemical reactions. The properties of specific keto acid depend upon the position of the keto group with reference to the carboxylic or other functional groups, such as 2-keto acids are generally less reactive because of the close proximity of keto group to the carboxylic function. Inductive effect and steric hindrance may be the cause of less reactivity of these keto groups.

Reactivity factors in the addition reaction of carbon heteroatom multiple bonds (C=N, C≡N, C=O) are similar to those of tetrahedral mechanism of nucleophilic substitution reaction. Since C=O bonds are strongly polar, with the carbon always the positive end, nucleophilic attacking species always go to the carbon and electrophilic to the oxygen. Reactions of carbon oxygen double bond are simple addition

with the reaction ending as soon as the two groups have been added. Electron-donating groups attached to keto function decrease the rate of reactions and electron-attracting substituents increase the rates. This means that aldehydes are more reactive than ketones.

In general it can be concluded that most of the reactions of keto functions are of two types.

1. $$R-\overset{\overset{O}{\|}}{C}-R' \xrightarrow{YH_2} R-\overset{\overset{YH}{|}}{\underset{\underset{OH}{|}}{C}}-R' \xrightarrow{-H_2O} R-\overset{\overset{Y}{\|}}{C}-R'$$

2. $$R-\overset{\overset{O}{\|}}{C}-R' \xrightarrow{YH_2} R-\overset{\overset{YH}{|}}{\underset{\underset{OH}{|}}{C}}-R' \xrightarrow{Z} R-\overset{\overset{YH}{|}}{\underset{\underset{Z}{|}}{C}}-R'$$

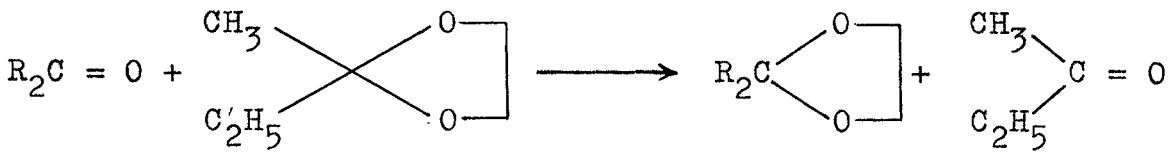
In recent years reactions of keto fatty acids have attracted attention for their academic and industrial interest. A number of long chain cyclic and non-cyclic keto acid derivatives such as oxazoles[1], thiazoles[1], tetrazoles[2], furan[3] and enol acetates[4] have been reported from our laboratory.

Condensation Reactions

Condensation of ethanedithiol, β-mercaptoethanol, ethylene-glycol or 1,2-propanediol with a variety of ketones is a method of ring formation[5-11] or protection[12] of the keto group under a variety of reaction conditions. However, the general

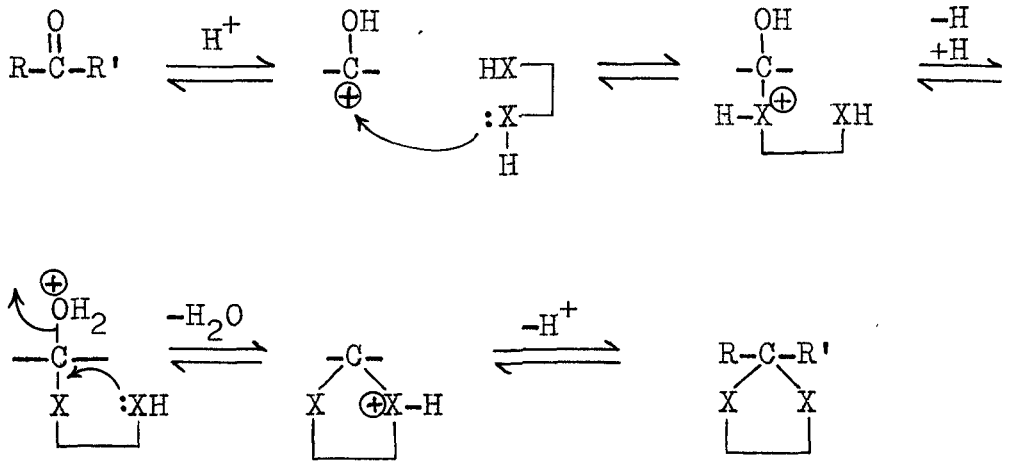
synthetic potentiality of this type of reactions has not been investigated in the field of fatty acid chemistry.

The condensation of ketones with β-mercaptoethanol and ethanedithiol was carried out in the presence of sodium sulfate and zinc chloride[5,6], hydrogen chloride in ether[7,8] and p-toluenesulfonic acid (p-TSA) in benzene under azeotropic conditions[9]. The exchange method[10] for the preparation of oxathiolanes involves a procedure, originally developed for ketals (dioxolanes), in which the ketone is refluxed in benzene with ethyl methyl ethylenedioxolane in the presence of p-TSA.



Later Fieser[13] prepared oxathiolanes and dithiolanes (thioketals) by using a more simple method, using borontrifluoride (BF_3)-etherate. The reaction occurs at room temperature involving mild conditions. In several instances, addition of BF_3-etherate to an acetic acid solution of ketones and excess of mercaptan at room temperature results in prompt separation of thioketals in high yield. An alternative procedure is to add BF_3-etherate to the suspension of ketones in β-mercaptoethanol or ethanedithiol.

The BF_3-etherate in this reaction thus acts as a Lewis acid and as a solvent. The reaction proceeds by the SN^1 mechanism as shown below.



This is a reversible reaction and ketals or hemithioketals can be hydrolyzed by treatment with acid, but are quite stable to bases. This makes it a useful method for protecting aldehydes and ketones under basic conditions. The reaction is of wide scope. Most of the aldehydes are easily converted to ketals with ketones the process is more difficult, presumably because of steric factors and the reaction often fails with cyclic ketones.

Dithiolanes, oxathiolanes and dioxolanes are more or less restricted to steroidal and short chain ketones. Recently these derivatives assumed importance on account of their pharmacological potentialities. Fatty acid derivatives containing ethyleneoxathiolane[14], substituted ethylene-oxathiolane[15] and ethylenedithiolane[16] ring systems were

successfully synthesized at auther's laboratory by the condensation of keto fatty acid esters with β-mercaptoethanol, 3-mercaptopropan 1,2-diol and ethanedithiol in the presence of BF_3-etherate and acetic acid respectively.

Discussion

Chapter 4.1

Synthesis of Long Chain Aromatic Dithiolanes

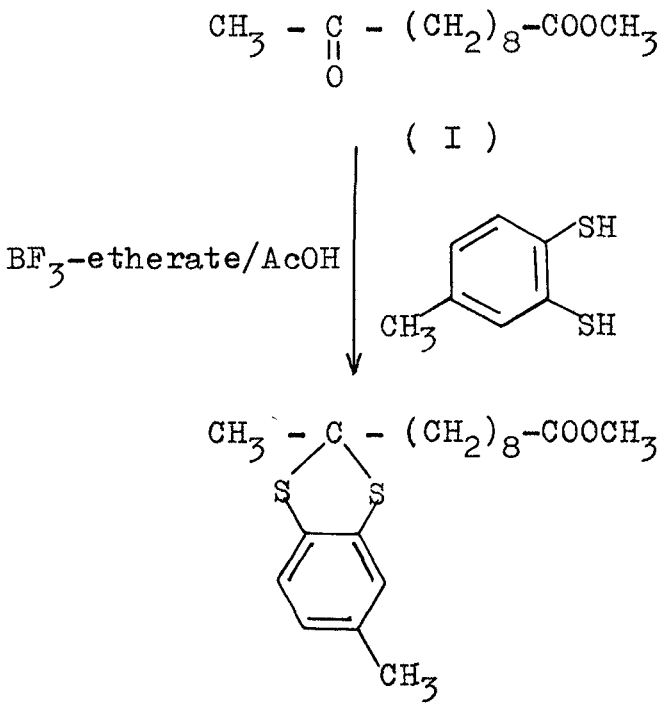
Dithiolanes have become of interest in recent years on account of their pharmacological potentiality[17]. Some dithiolanes have been identified as components of the anal gland secretions of the ferret[18]. Isoprothiolanes and related compounds have been identified as a controller of rice blast caused by Pyricularia oryzae and planthoppers[19]. Several chlorine-containing dithiolanes have been found to be effective as herbicides[20] and been held responsible in producing antifertility effect in male rats[21]. The recent reports have recognized some of the dithiolanes as choleretic and hepatoprotective[22] and also as radioprotectant[23,24]. The dithiolanes, containing aromatic ring have been used in the preparation of several anticancer pharmaceuticals[25].

The general synthetic potentiality and generality of dithiolanation reaction in the field of fatty acid chemistry has recently been studied in our laboratory[16]. With a view to prepare some new dithiolane fatty derivatives containing aromatic ring, an attempt has been made to condense various oxo acids/esters with toluene 3,4-dithiol in the presence of

acetic acid and BF_3-etherate.

Reaction of Toluene-3,4-dithiol with Methyl 10-oxoundecanoate(I)

Methyl 10-oxoundecanoate (I) was prepared by oxymercuration-demercuration[26] followed by Jones' oxidation[27] and esterification of 10-undecenoic acid. This oxo ester was allowed to react with toluene-3,4-dithiol in the presence of BF_3-etherate and acetic acid as described by Fieser[13]. Final work up and purification by column chromatography yielded VIII as a viscous oil.



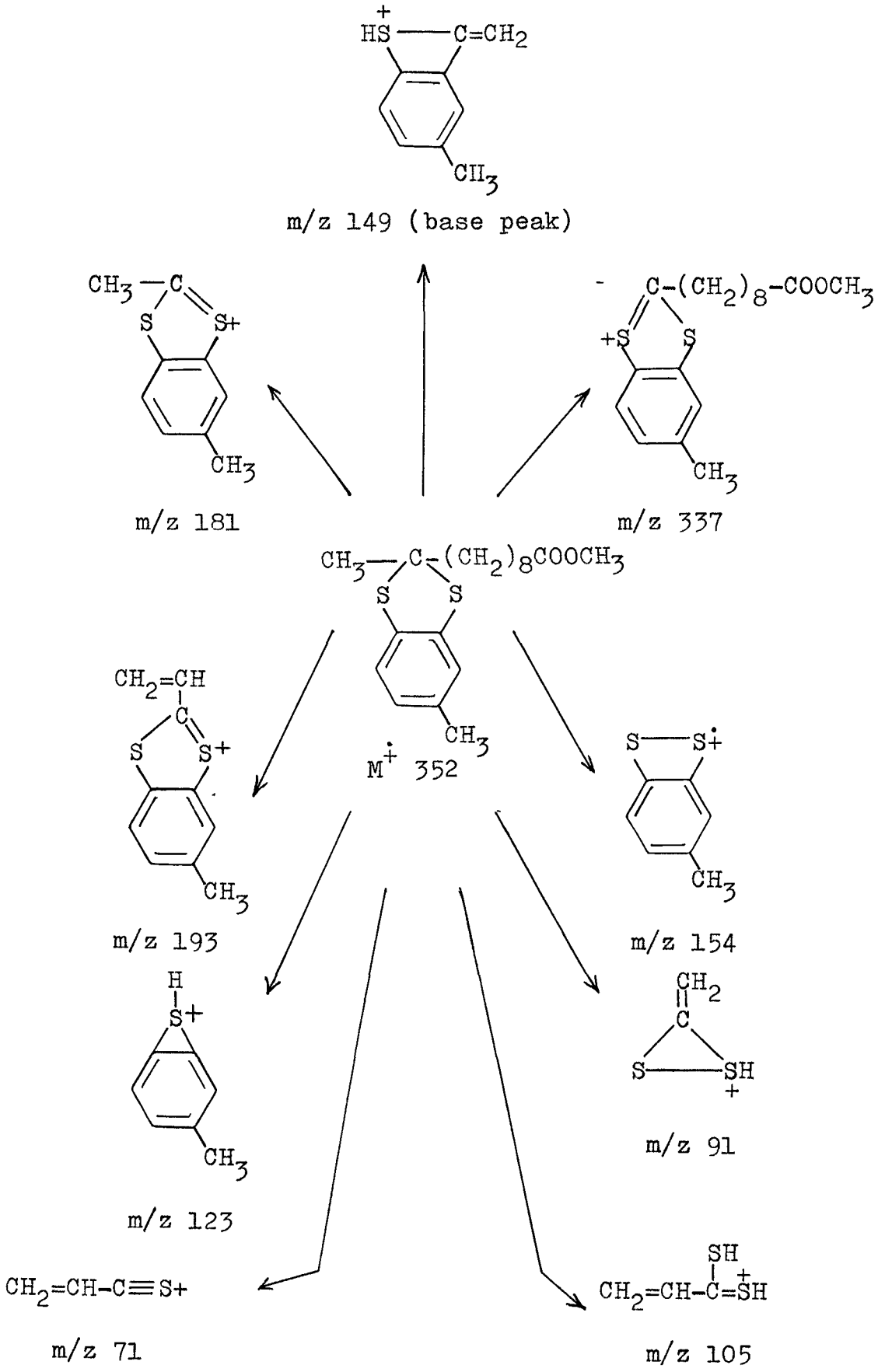
(VIII)

Characterization of the Product (VIII)

The compound (VIII) was analyzed for $C_{19}H_{28}O_2S_2$. IR spectrum of this compound showed no band for free oxo group (1720 cm^{-1}). The condensation of toluene-3,4-dithiol with oxo function was evidenced by the appearance of bands at 3070 (C-H stretching; aromatic), 1590 (C=C stretch.; aromatic) and 820 cm^{-1} (out of plane bending of ring C-H bond). The band for ester carbonyl was observed at 1735. The NMR spectrum showed the diagnostic signals at δ 6.65-7.1 br m centred at 6.9 for three aromatic protons and 2.22 as sharp singlet of the methyl protons of toluene. Terminal methyl protons and C9-methylene protons absorbed at 1.78 s and 2.09 t respectively, which indicates the incorporation of the dithiolane ring at C10. The other usual signals appeared at 3.58 s ($-COOCH_3$), 2.3 (methylene protons α-to ester carbonyl) and 1.3 (chain methylene protons). These data supported the formulation of VIII as methyl 10,10-toluene-3,4-disulfideundecanoate.

The spiro formulation of product (VIII) was substantiated by a study of its mass spectrometry (Scheme 1, Fig. 1). The mass ion at m/z 352 corresponded to the molecular weight and confirmed the microanalysis. The diagnostic mass ions at 337 and 181 arising from α-cleavages to ring established the nature and position of the ring at C10. A characteristic mass ion at 193 was observed in the spectrum. Such type of fragment ion had earlier been reported as characteristic

Scheme 1


m/z 149 (base peak)
m/z 181
m/z 337
M+ 352
m/z 193
m/z 154
m/z 123
m/z 91
m/z 71
m/z 105

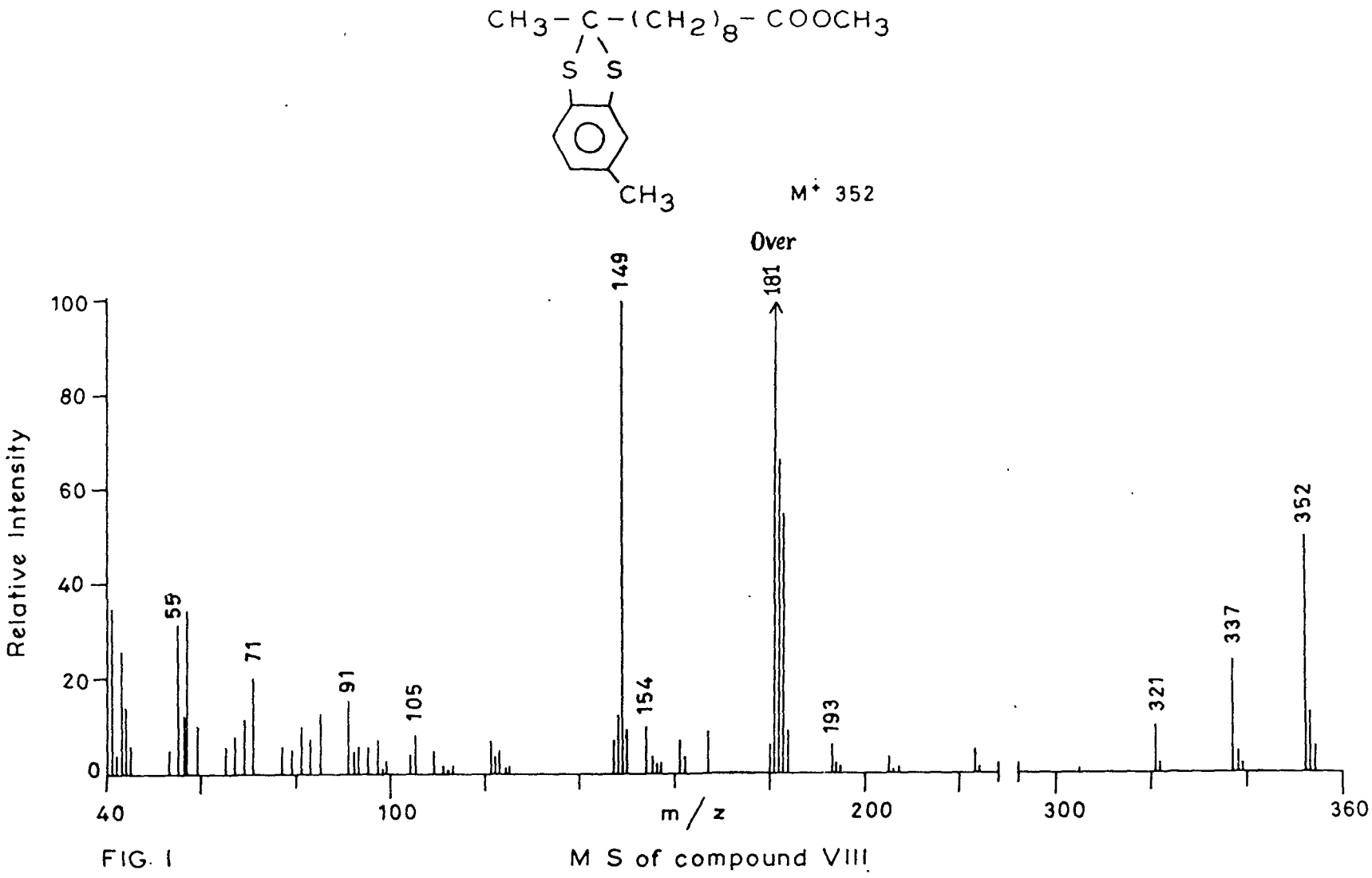
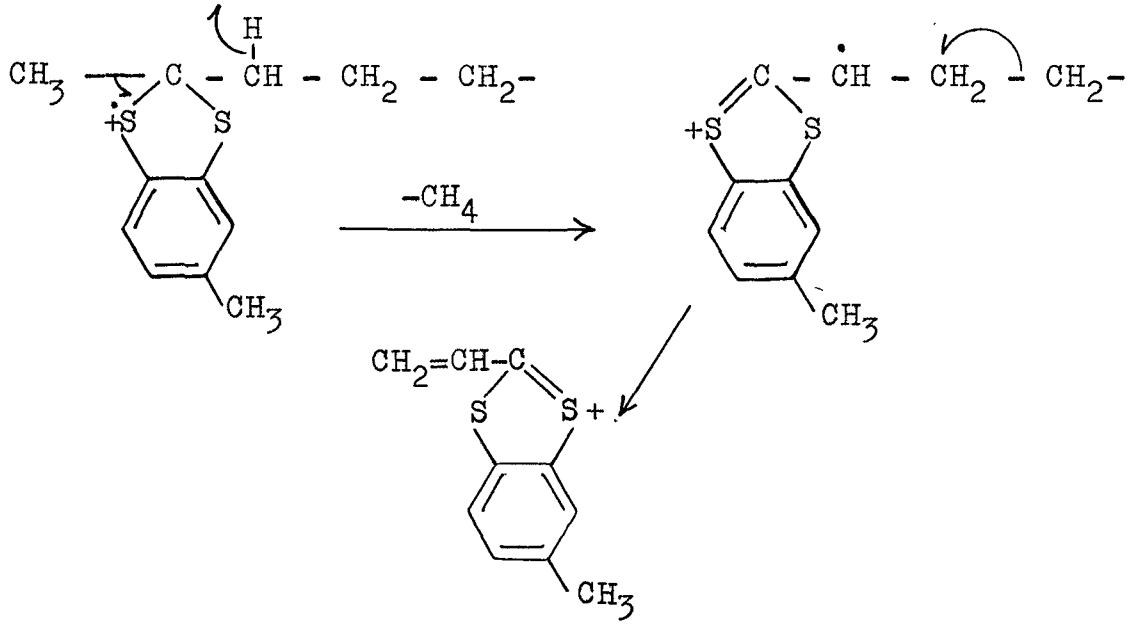


FIG. I M S of compound VIII

of the dithiolane grouping[28]. The genesis of this diagnostic ion 193 required α-cleavage on one side and γ-cleavage from another side of the dithiolane ring accompanied by hydrogen transfer as shown in scheme indicated below.



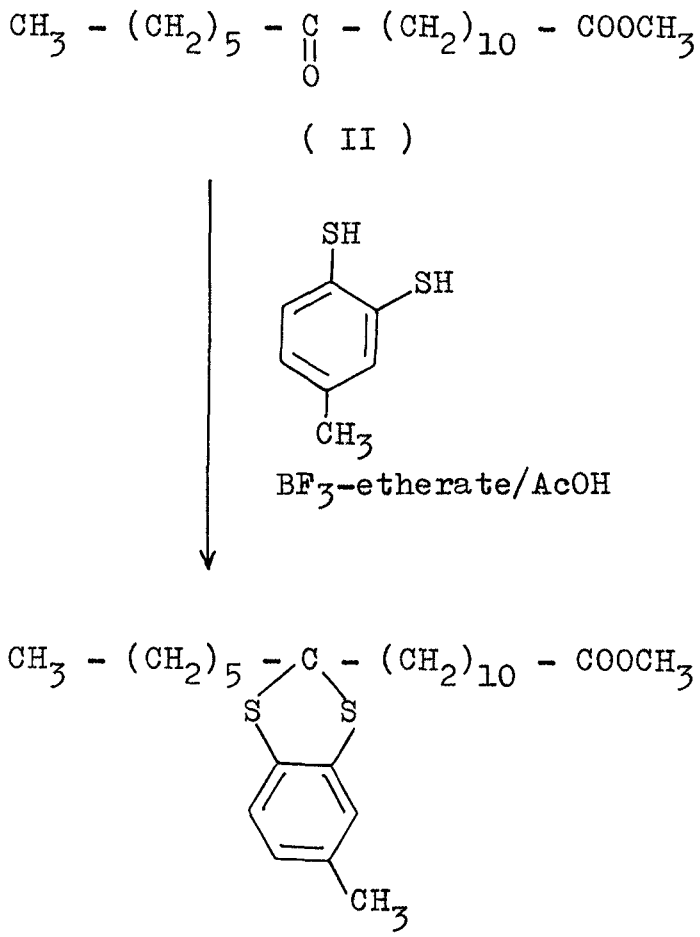
m/z 193

Other salient mass ions observed at 353 (M+H), 354 (M+2H), 338 (337+H), 339 (377+2H), 321 (M-OCH_3), 322 (321+H), 323 (321+2H), 305 (337-CH_3OH), 223 (181+C_3H_6), 182 (181+H), 183 (181+2H), 167 (193-26), 161 (193-32), 123 and lower mass ions at 105, 91, 71, 57 and 43. The peak at 71 is thought to be formed from fragmentation of the mass ion 193[28].

Reaction of Toluene-3,4-dithiol with Methyl 12-oxooctadecanoate (II)

12-Hydroxyoctadec-cis-9-enoic (ricinoleic) acid was isolated from Ricinus communis seeds and was hydrogenated to get

12-hydroxyoctadecanoic acid. Its Jones' oxidation[27] followed by esterification yielded methyl 12-oxooctadecanoate (II). This oxo ester on treatment with toluene-3,4-dithiol, BF_3-etherate and acetic acid yielded IX as a viscous oil.



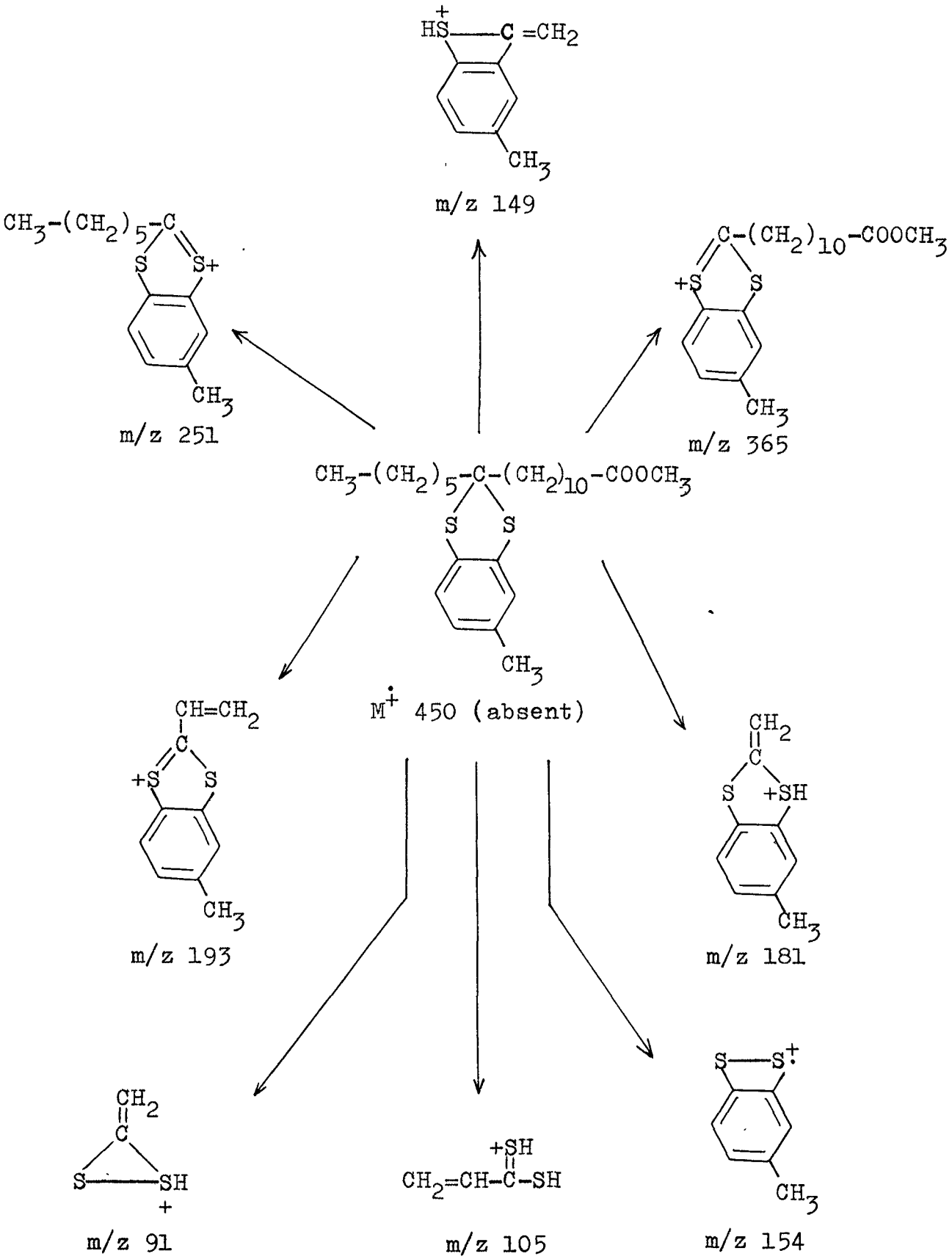
Characterization of the Product (IX)

Elemental analysis of the product (IX) corresponded to the formula $C_{26}H_{42}O_2S_2$. The nonexistence of a band at 1710 cm^{-1}

in IR spectrum and negative DNP test indicated the condensation of oxo function with the reagent. The bands at 3060, 1585 and 810 suggested the presence of aromatic ring in the molecule. Its NMR spectrum exhibited a three proton ill defined multiplet centred at δ 6.87 (aromatic protons) and a sharp singlet at 2.26 (methyl protons of toluene). Another six proton multiplet appeared at 2.05 attributable to C11-,C13-(α-to ring) and C2-(α-to ester carbonyl) methylene protons which merged in part with methyl protons of the toluene ring. Other usual signals observed at 3.62 s ($-COOCH_3$), 1.33 (chain methylene protons) and 0.9 t (terminal methyl protons). These data suggested the structure of IX as methyl 12,12-toluene-3,4-disulfide-octadecanoate.

Mass spectrum corroborated the structure of IX by showing parent ion peak at m/z 365 (cleavage α-to ring of the ester side), from which the mass ion 334 emerges by the elimination of OCH_3 (Scheme 2, Fig. 2). Another characteristic peak at 251, arising from α-cleavage of the alkyl chain side, established the position of ring at C12. The other significant fragments observed at 366 (365+H), 367 (365+2H), 252 (251+H) and 253 (251+2H) originate from α-cleavage with concomitant one and/or two hydrogen transfer towards ring, and thus support the structure. Other prominent mass fragments were observed at 363 (M-87), 291 (365-74), 278 (365-87), 223 ($251-C_2H_4$), 193 (characteristic of dithiolane grouping)[28],

Scheme 2



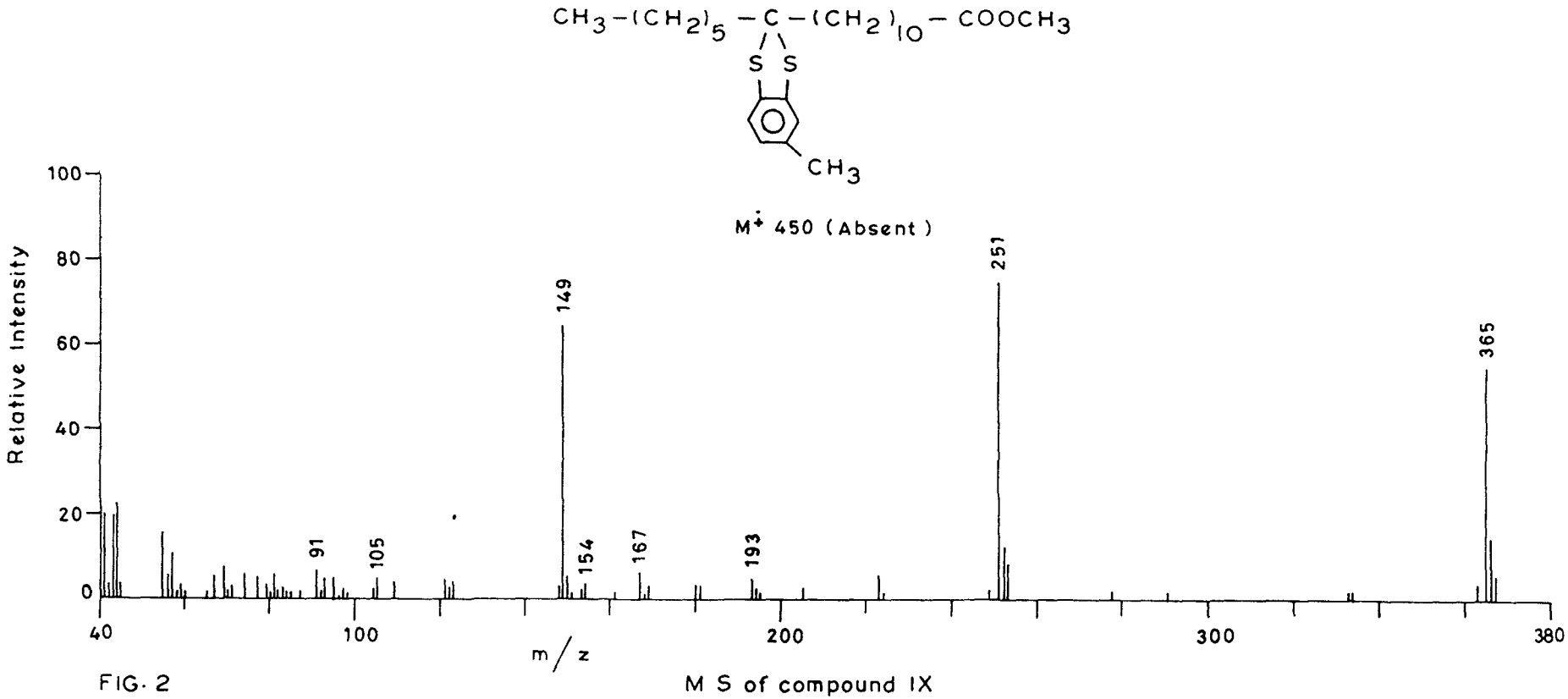
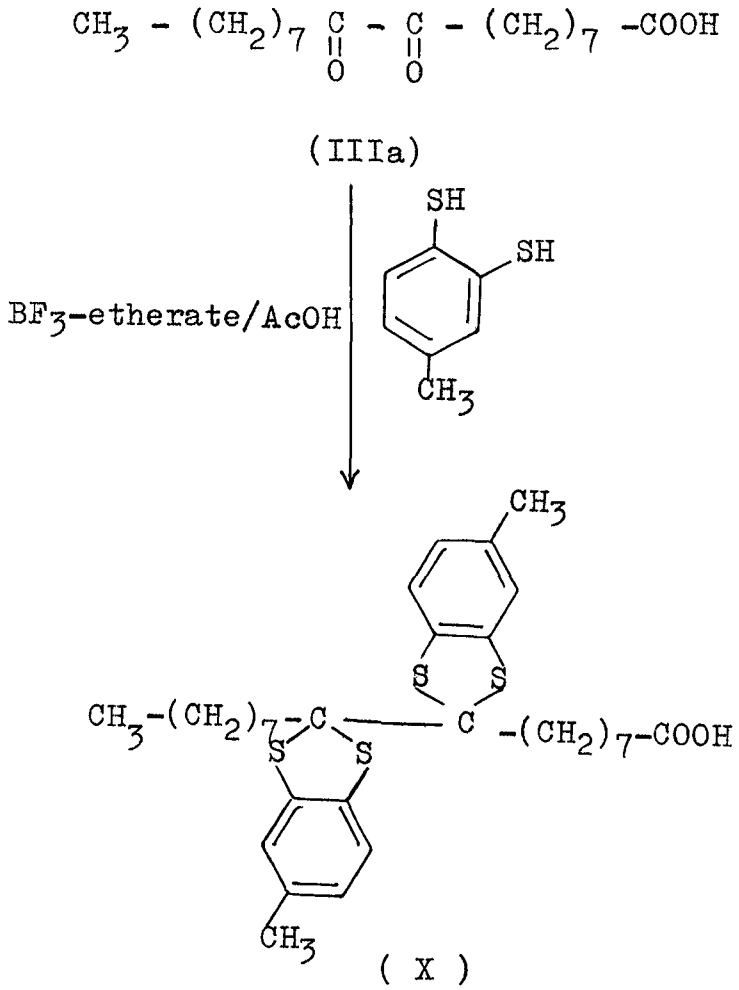


FIG. 2 M S of compound IX

180, 167 (193-26), 161 (193-32), 154, 149, 123, 105, 91, 55 and 40 (base peak).

Reaction of Toluene-3,4-dithiol with 9,10-Dioxooctadecanoic Acid (IIIa)

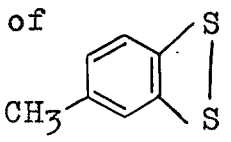
9,10-Dioxooctadecanoic acid (IIIa) was prepared by $KMnO_4$ hydroxylation of octadec-cis-9-enoic (oleic) acid followed by N-bromosuccinimide (NBS) oxidation[29]. This oxo acid was allowed to condense with toluene-3,4-dithiol in a similar way as described earlier. Usual work up and resolution by column chromatography yielded a thick oily product (X).



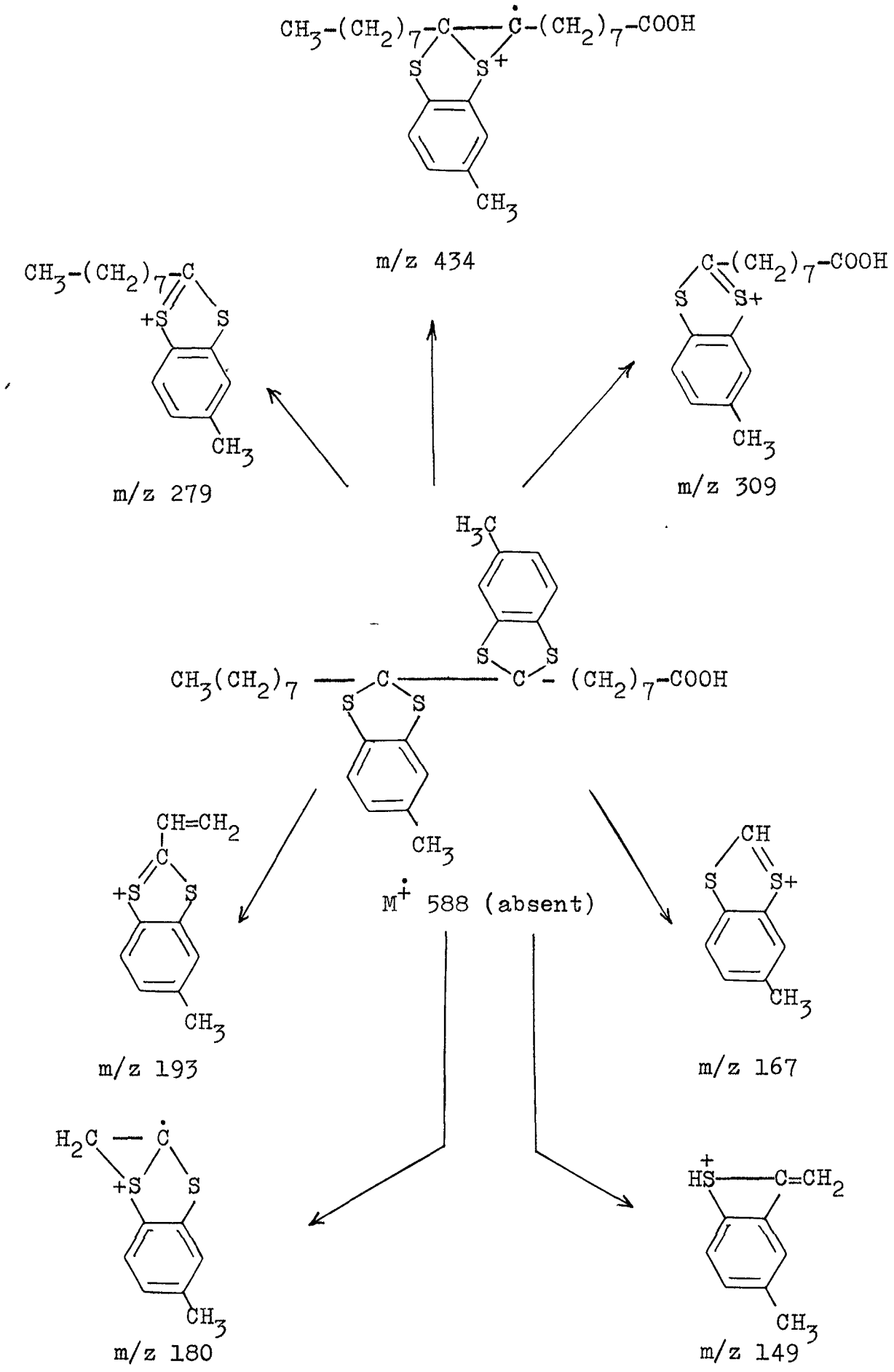
(X)

Characterization of the product (X)

The elemental analysis of X corresponded to the formula $C_{32}H_{44}O_2S_4$. Its IR spectrum gave bands at 3030, 1590 and 860 cm^{-1} (aromatic ring). There was no evidence of free carbonyl band . The NMR spectrum was found to be more informative in the elucidation of structure of the compound (X) by counting the aromatic protons. Its NMR spectrum exhibited two proton broad multiplet at δ 7.3 (C5-aromatic proton of two toluene rings) and 6.78 as multiplet for four protons (C2- and C6-aromatic protons of the rings). A diagnostic signal at 2.1 for twelve protons ascribable to C2-, C8- and C11-methylene protons α-to ester and dithiolane rings merged with methyl protons of the two toluene rings was another clue in favor of the incorporation of the two rings. These data were in confirmity with the structure of X formulated as 9,9,10,10-bis-toluene-3,4-disulfideoctadecanoic acid.

Mass spectrum of this compound (Scheme 3, Fig. 3) agreed with the structure by showing the peaks at m/z 309 and 279 arising from the rupture of C9-C10 bond between the two dithiolane rings. These two characteristic fragments established the position of rings at C9 and C10. A mass ion at 434 arising due to the loss of  (molecule 154)

Scheme 3



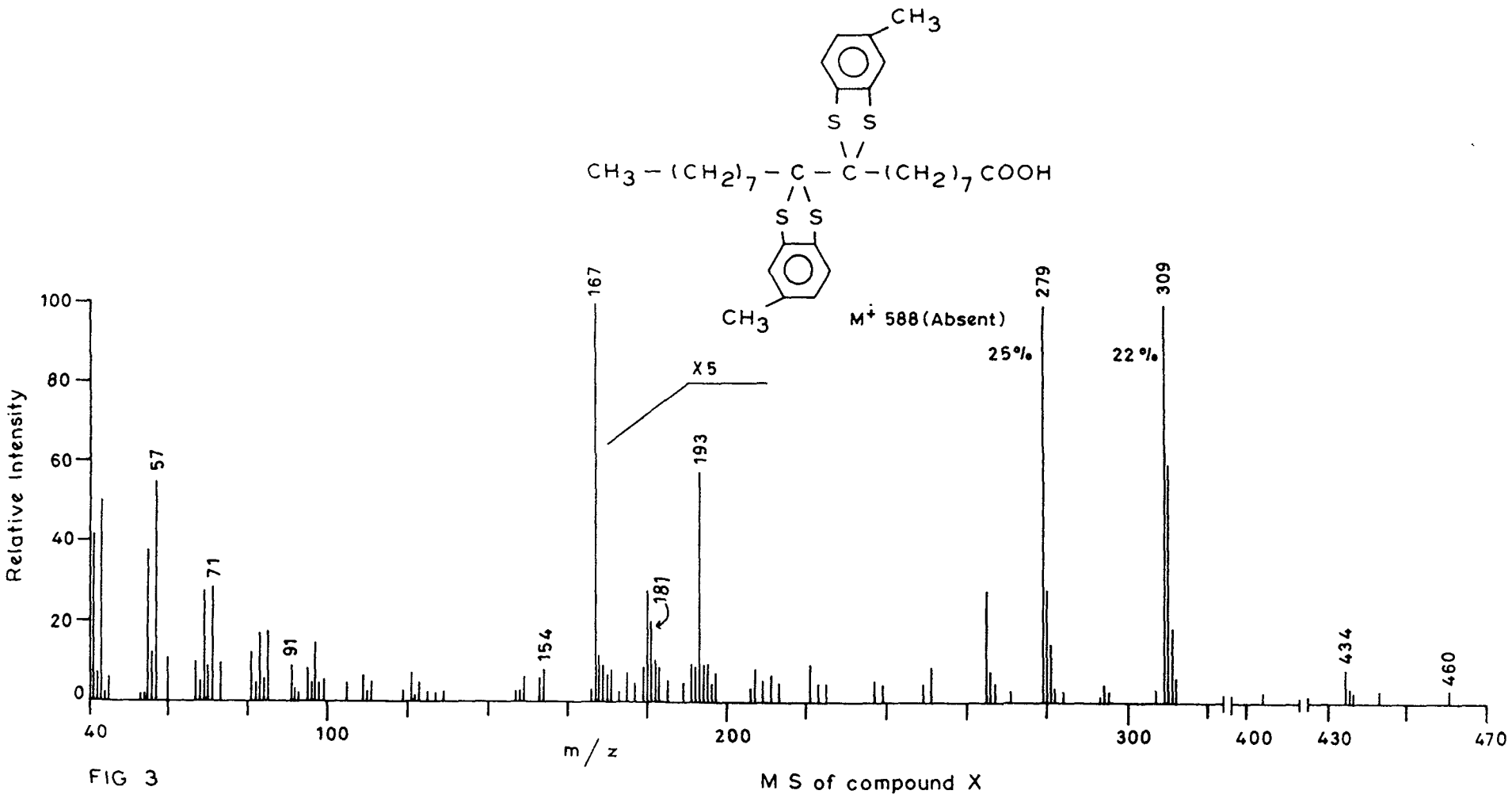


FIG 3

M S of compound X

from molecular ion identified the dithiolanic nature of the ring. A mass ion at 460 arising due to the loss of $CH_3-(CH_2)_7$ from molecular ion followed by the elimination of methyl group from one dithiolane ring confirmed the simultaneous condensation of both oxo groups with toluene-3,4-dithiol. This mass fragment further eliminated -OH group and formed mass ion 443. The other significant mass ions were observed at 436 (434+2H), 404(436-S), 310 (309+H), 311 (309+2H), 280(279+H) and 281 (279+2H). The other salient mass ions present were 291 ($309-H_2O$), 265 ($280-CH_3$), 251 ($279-C_2H_4$), 237 ($279-C_3H_6$), 235, 221 ($235-CH_2$), 207 ($221-CH_2$), 193, 181, 167 (base peak), 154, 149, 123 and lower mass ions at 105, 91, 71, 57, 55 and 43.

Reaction of Toluene-3,4-dithiol with 9-Oxooctadec-cis-12-enoic Acid (IV)

9-Oxooctadec-cis-12-enoic acid (IV) was prepared (by the method of Nichols and Schipper[30], chromic acid oxidation) from the mixed fatty acids isolated from Wrightia tinctoria seed oil by refluxing with ethanolic KOH followed by acidification with dil. HCl. The reaction was completed in one hr only. After final work up and crystallization with alcohol afforded 9-oxooctadec-cis-12-enoic acid (IV, mp. 44-45 C).

Mixed Fatty Acids

↓ Sodium dichromate dihydrate, CH_3COOH and H_2SO_4 R.T. 1 hr stirring

$$CH_3-(CH_2)_4-CH=CH-CH_2-CH_2-\underset{\underset{O}{\|}}{C}-(CH_2)_7-COOH$$

(IV)

Microanalysis of IV corresponded to formula $C_{18}H_{32}O_3$ and gave following spectral data: IR [(cm^{-1}) 1720 (free carbonyl), 1705 (acid carbonyl)]; NMR [(δ) 5.28 m (2H,-CH=CH-), 2.3 br m (8H, C2-, C8-, C10- and C11-methylene protons), 2.05 m (2H, C14-methylene protons), 1.33 and 0.9] and MS [(m/z) M^+ 296, McLafferty fragments at 186 and 168 (Fig. 4), mass ions due to α-cleavage at 171, 153, 125 and other salient peaks at 111, 185 (β-cleavage), 97 (111-CH_2), 83, 69]. All taken together established the structure of IV as 9-oxooctadec-cis-12-enoic acid.

This oxo acid was allowed to react with toluene-3,4-dithiol in the presence of acetic acid and BF_3-etherate. After final work up and column chromatographic separation two TLC homogeneous oily products were obtained (XI and XII).

Characterization of the Major Product (XI)

The compound was analyzed for $C_{25}H_{38}O_2S_2$. The IR spectrum displayed bands at 3030, 1585 and 860 cm^{-1} (aromatic ring). A weak band at 1620 was also observed which was attributable to olefinic bond. These bands indicated the presence of dithiolane ring and double bond in the molecule. The band for acid carbonyl appeared at 1700. The NMR spectrum gave conclusive support in favor of structure XI by displaying characteristic signals at δ 6.88 as broad multiplet accountable for three aromatic protons, at 2.22 as sharp singlet for methyl

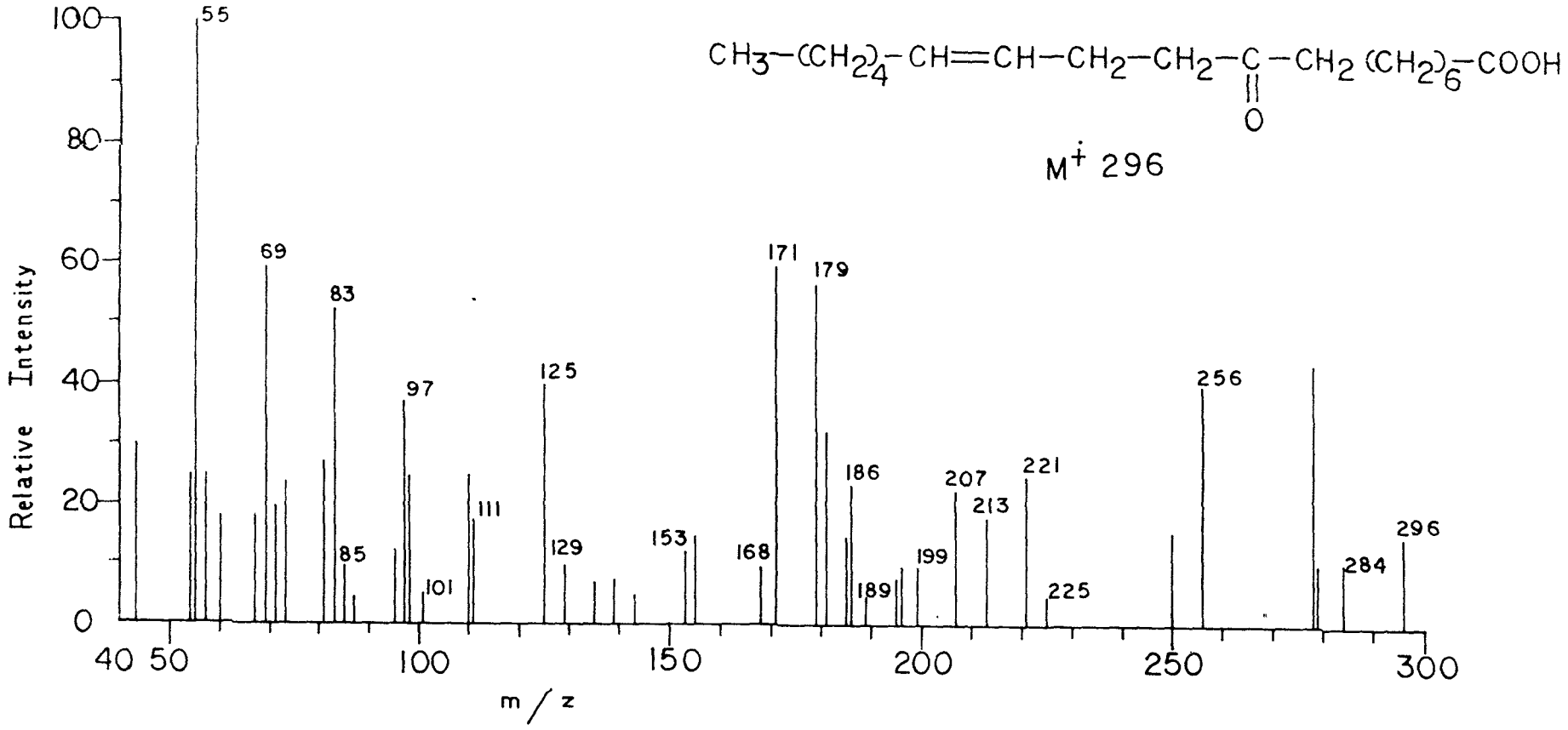
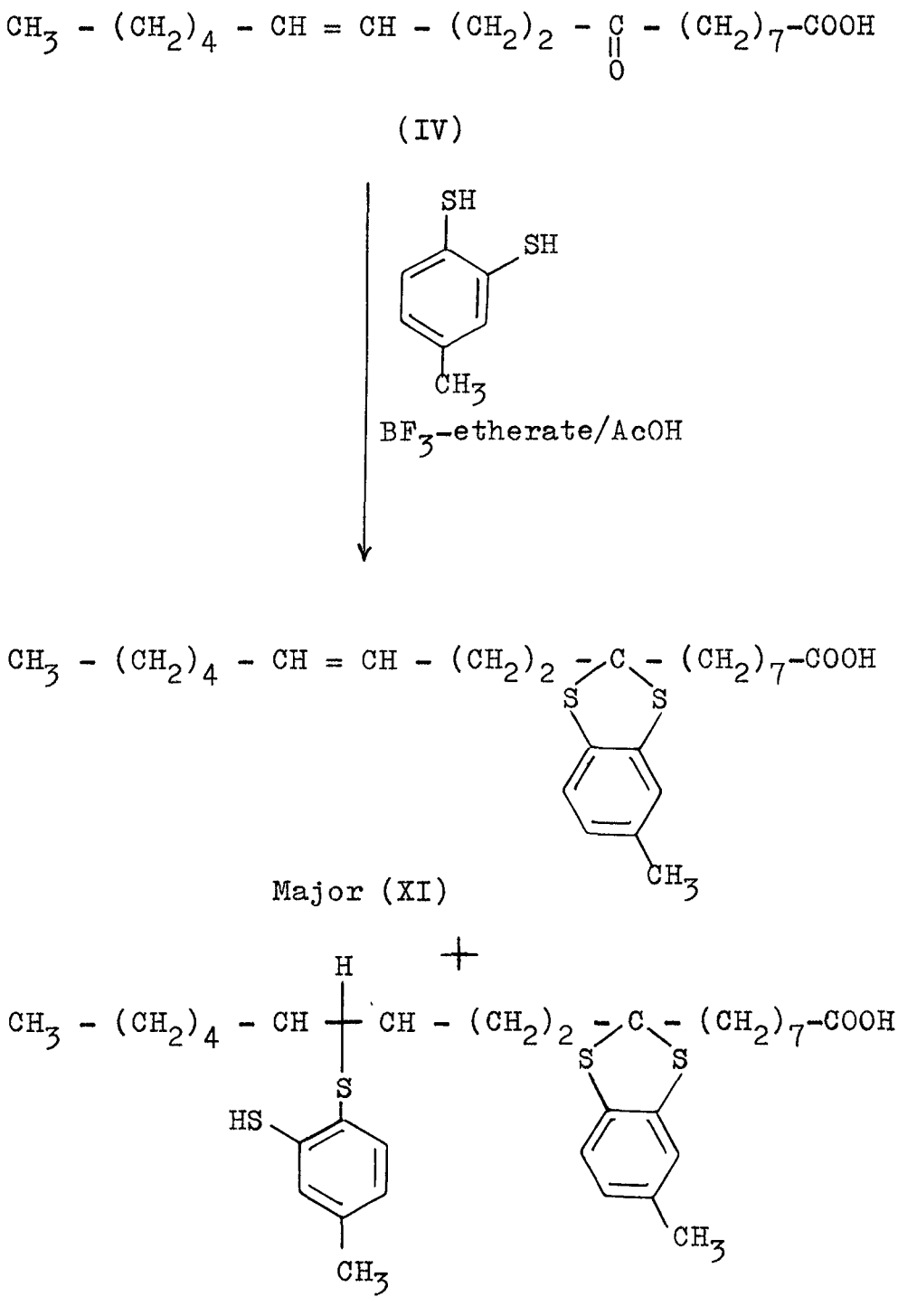


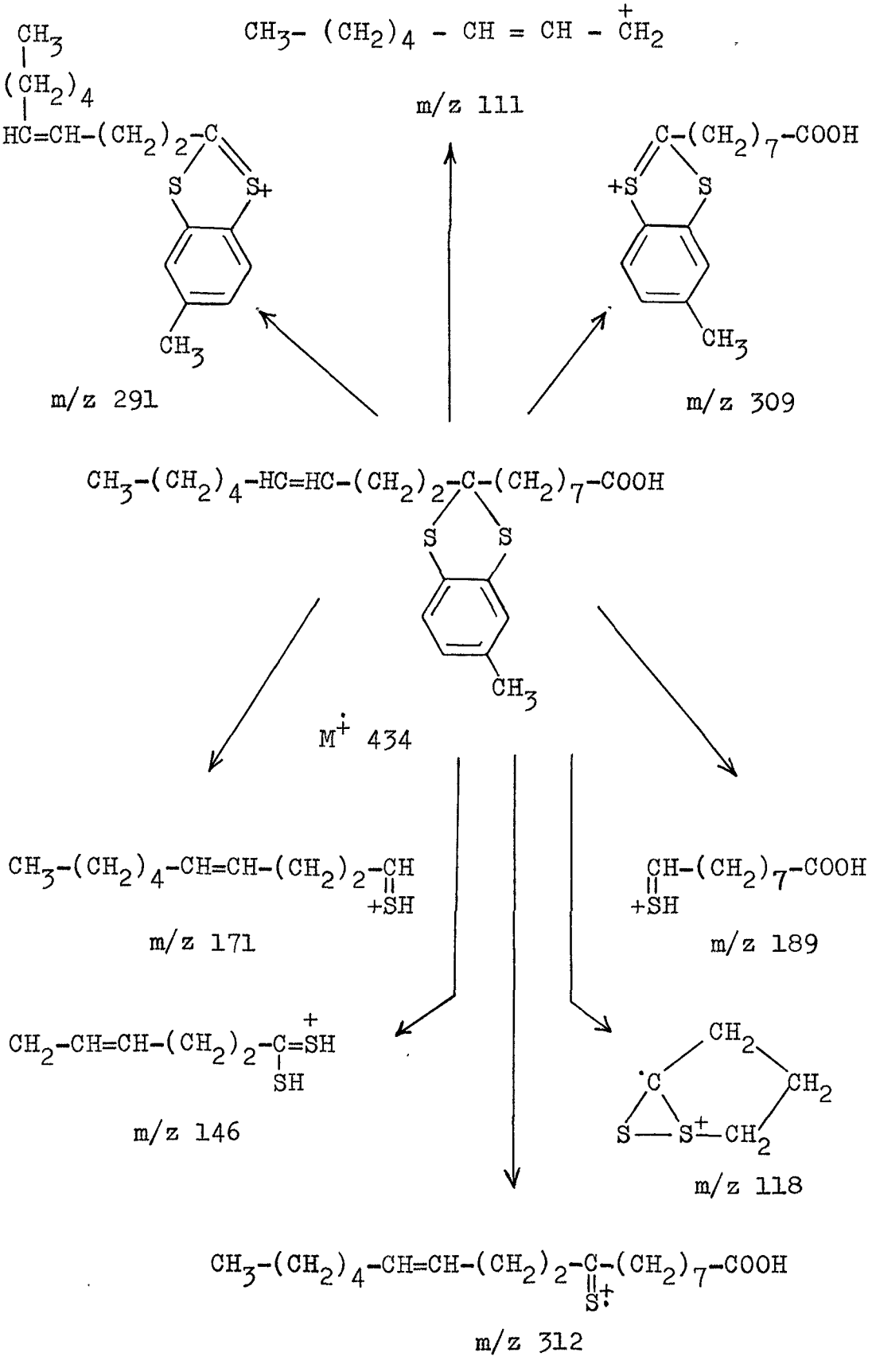
FIG.4 MS of compound IV


CH3 - (CH2)4 - CH = CH - (CH2)2 - C - (CH2)7-COOH
O
(IV)
SH
SH
CH3
BF3-etherate/AcOH
CH3 - (CH2)4 - CH = CH - (CH2)2 - C - (CH2)7-COOH
S
S
CH3
Major (XI)
+
H
CH3 - (CH2)4 - CH
CH - (CH2)2 - C - (CH2)7-COOH
S
HS
CH3
S
S
CH3
Minor (XII)

protons of toluene and at 5.3 as a multiplet of C12-vinylic protons. A multiplet signal appeared at 2.08 for ten protons of C2-, C8-, C10-, C11- and C14-methylene groups, α-to acid carbonyl, dithiolane ring and double bond. These signals merged in part with the methyl protons of the ring. These spectral data confirmed the structure of compound (XI) as 9,9-toluene-3,4-disulfideoctadec-cis-12-enoic acid.

The MS of XI further supported the structure (Scheme 4, Fig. 5). It had small molecular ion peak at m/z 434 along with 435 (M+H) and 436 (M+2H). The most characteristic mass ions at 309 and 291 due to α-cleavage of both sides to ring confirmed the toluenedithiolane ring at C9 and one double bond in the chain. The mass ion 291 may be due to the elimination of the water molecule from the ion 309. The diagnostic fragment ion 111 resulted due to allylic cleavage which confirmed the position of double bond between C12 and C13. A mass ion at 312 was obtained by the removal of toluenesulfide from the molecular ion. It further fragmented to give ions at 171, 185 (171+CH_2), 199 (185+CH_2), 213(199+CH_2), 227 (213+CH_2) and 241 (227+CH_2). The characteristic mass ions of the ring were observed at 193, 181, 180, 167, 154, 149, 123, 105, 91 and 71. The other salient mass ions were present at 294 (312-H_2O), 256 (291-[H_2S+H]), 189, 146, 129 (189-60), 118, 115 (129-CH_2), 101 and lower mass ions at 87, 73, 60, 55 and 40 (base peak).

Scheme 4


CH3-(CH2)4-CH=CH-CH2+
m/z 111
m/z 291
m/z 309
CH3-(CH2)4-HC=HC-(CH2)2-C-(CH2)7-COOH
M+ 434
CH3-(CH2)4-CH=CH-(CH2)2-CH
+SH
m/z 171
CH-(CH2)7-COOH
+SH
m/z 189
CH2-CH=CH-(CH2)2-C=SH+
SH
m/z 146
m/z 118
CH3-(CH2)4-CH=CH-(CH2)2-C-(CH2)7-COOH
S+
m/z 312

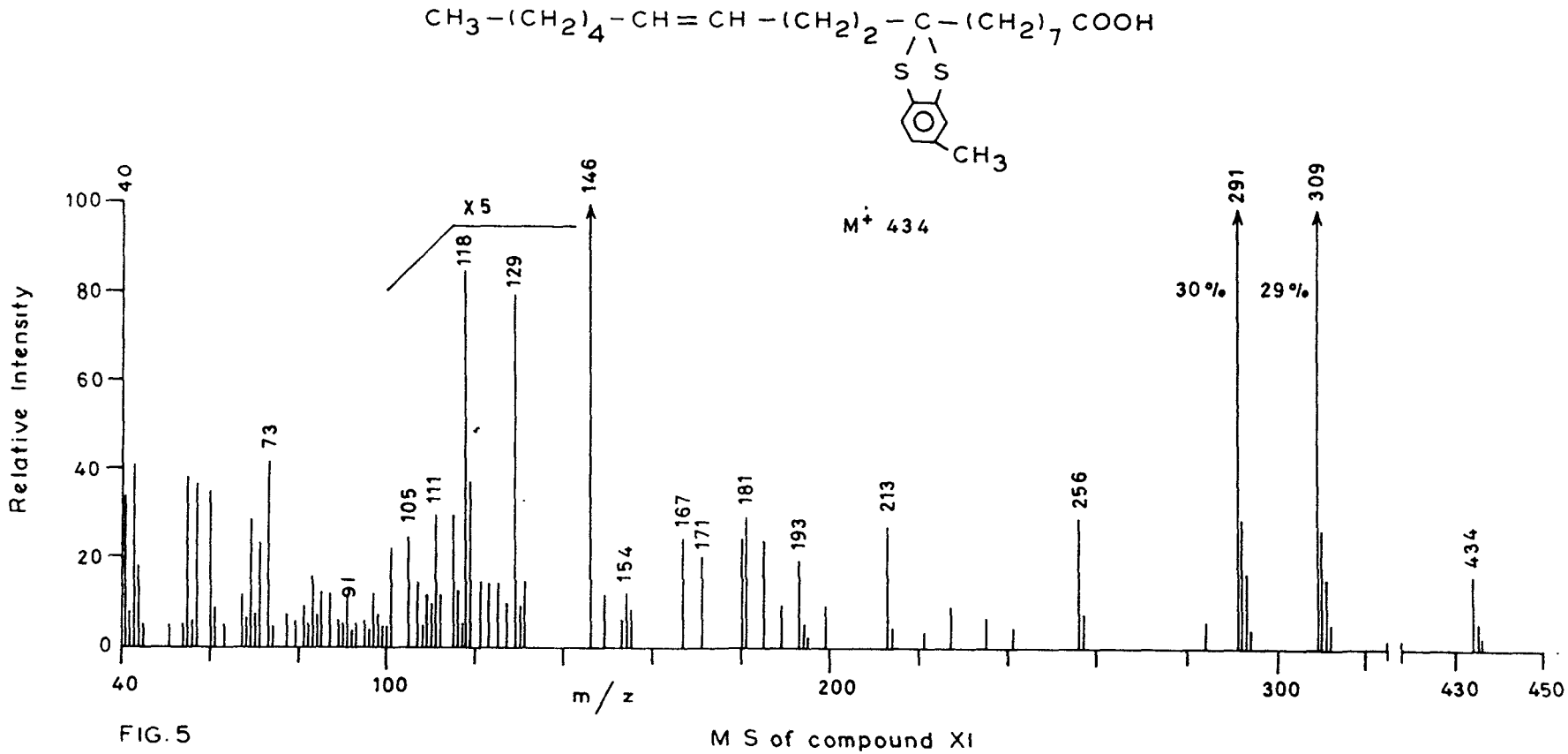
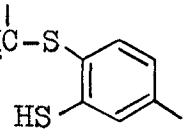


FIG. 5

M S of compound XI

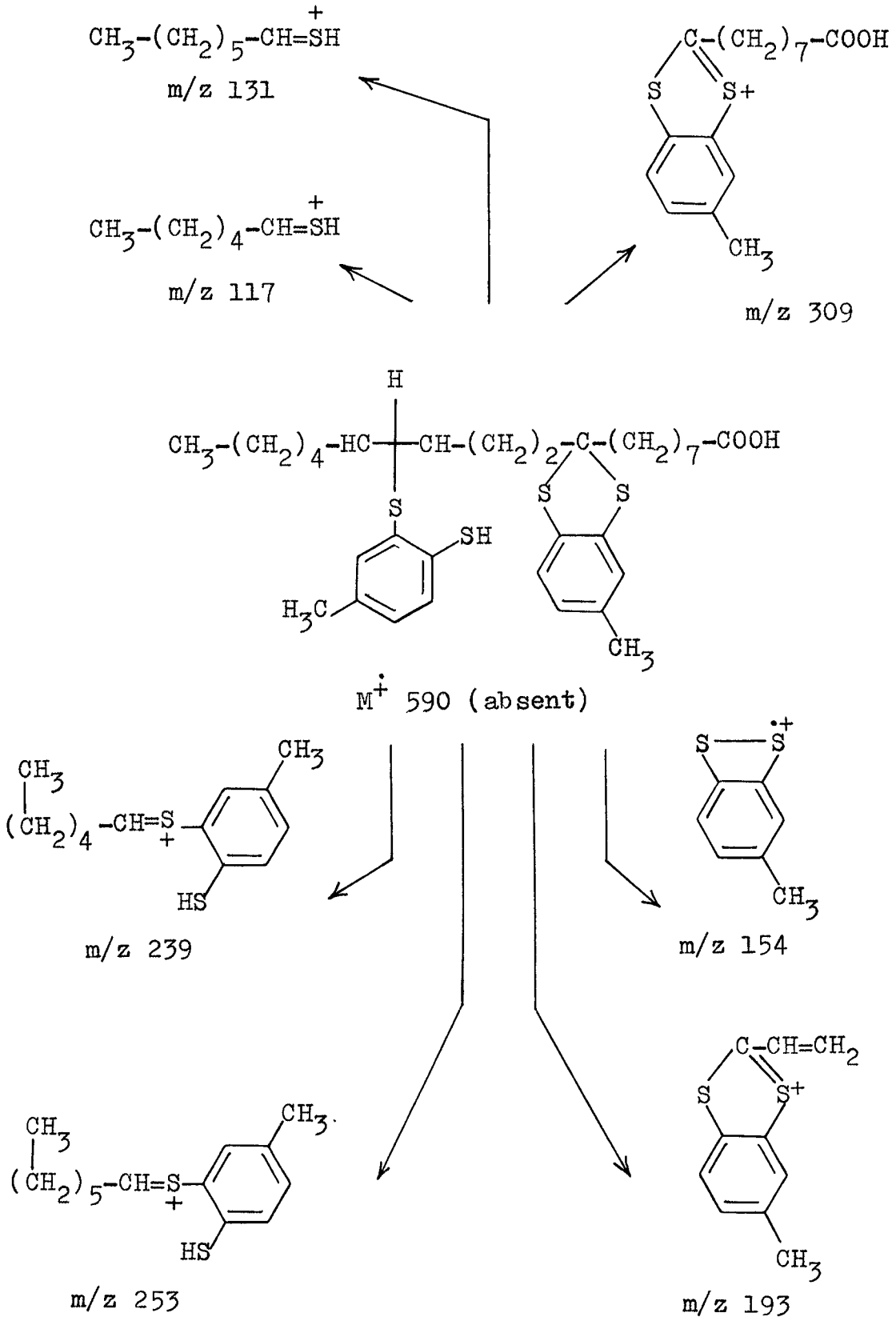
Characterization of the Minor Product (XII)

The liquid product (XII) on microanalysis showed the formula $C_{32}H_{46}O_2S_4$. The IR spectrum exhibited bands at 3040, 1590, 850 (aromatic ring) and 1710 cm^{-1} (COOH). Its NMR spectrum showed signals of significance. It showed two multiplets at δ 7.3 (2H) and 6.88 (4H) for C5- and C2-, C6-protons of both aromatic rings respectively. Formation of thioether by the addition of toluene-3,4-dithiol to the double bond was suggested by the appearance of NMR signals at 3.1 (1H, 

and 1.9 (-SH). On the basis of the above data the product (XII) was characterized as 9,9-toluene-3,4-disulfide-12(13)-[4(3)-thiol toluene-3(4)-mercapto] octadecanoic acid.

An additional support for the above structure was obtained from the study of its mass spectrum (Scheme 5, Fig. 6). The molecular ion peak was not observed. Fragment m/z 309 confirmed the dithiolane ring at C9. The formation of thioether at C12 and C13 was further confirmed by the appearance of fragment ions at 239 and 253. The loss of toluenesulfide from these ions resulted in the formation of fragment ions 117 (base peak) and 131 respectively. The other significant peaks were observed at 322 [(309+C_2H_4)-CH_3], 291 (309-H_2O), 276 (291-CH_3 or 432-156), 244 (276-S), 193, 186 (309-123), 181, 167 (193-26), 154, 149, 146, 121 (154-SH), 119 (117+2H), 91 and 71.

Scheme 5


CH3-(CH2)5-CH=SH+
m/z 131
CH3-(CH2)4-CH=SH+
m/z 117
C-(CH2)7-COOH
S
S+
CH3
m/z 309
H
CH3-(CH2)4-HC-CH-(CH2)2-C-(CH2)7-COOH
S
SH
H3C
S
S
CH3
M+ 590 (absent)
CH3
(CH2)4-CH=S+
HS
m/z 239
S
S+
CH3
m/z 154
CH3
(CH2)5-CH=S+
HS
m/z 253
C-CH=CH2
S
S+
CH3
m/z 193

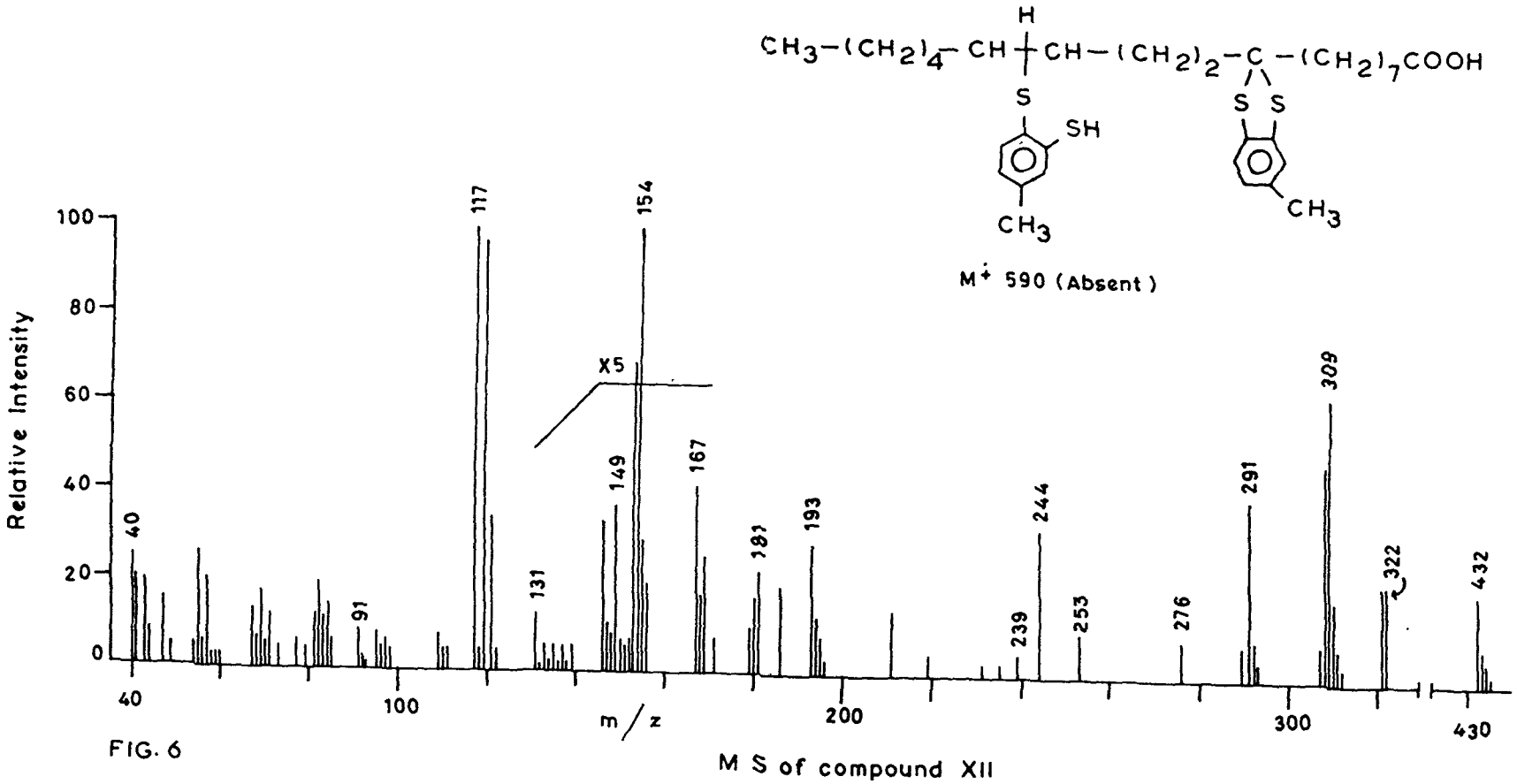


FIG. 6

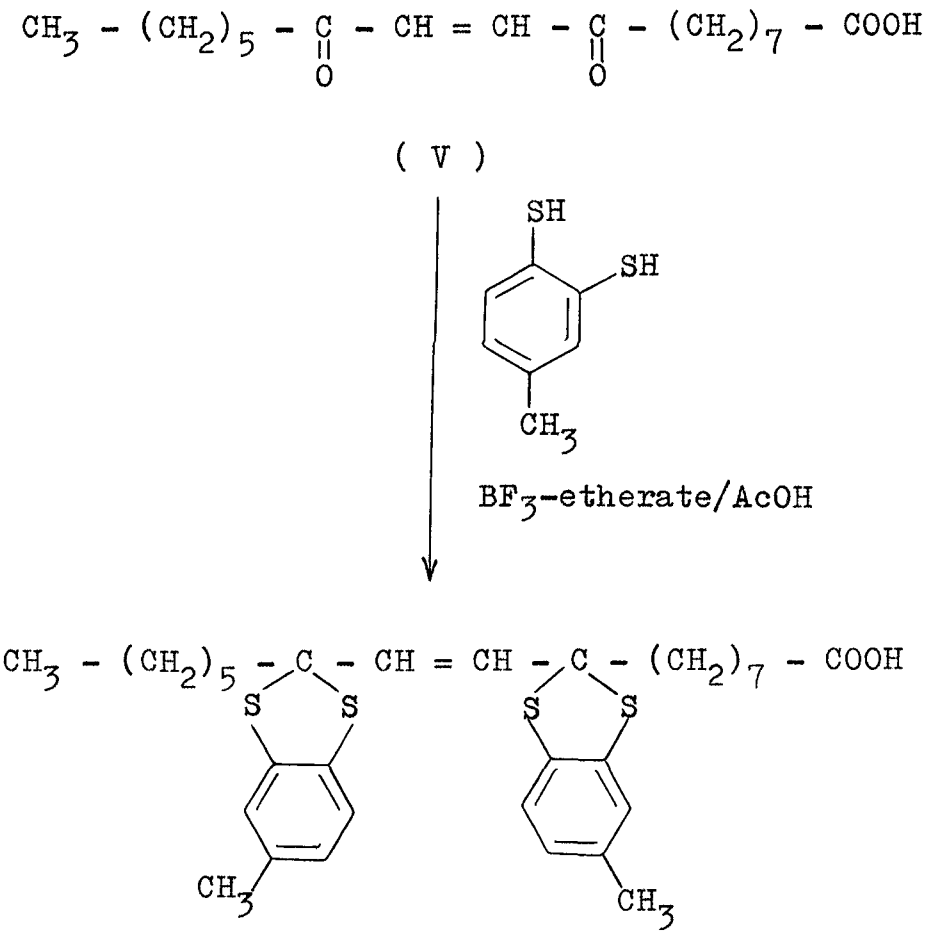
M S of compound XII

Reaction of Toluene-3,4-dithiol with 9,12-Dioxooctadec-*trans*-10-enoic Acid (V)

Castor fatty acids were extracted from seeds of *Ricinus communis* and were oxidized in the presence of sodium dichromate dihydrate, acetic acid and conc. sulfuric acid as described by Gunstone et al.[31] After the fall of temperature (~8 C) another set of oxidizing agent was added and the reaction mixture was stirred for an hr. The dioxo acid precipitated after addition of ice cold water. After crystallization from aqueous ethanol 9,12-dioxooctadec-*trans*-10-enoic acid (mp. 111 C) was obtained. This oxo acid was allowed to react with toluene-3,4-dithiol in the presence of acetic acid and BF_3-etherate. The work up of the reaction mixture yielded two products (XIII and XIV).

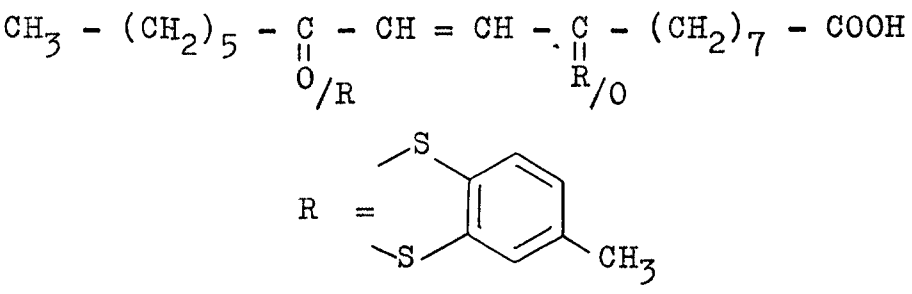
Characterization of the Product (XIII)

Microanalysis of the product (XIII) gave the composition as $C_{32}H_{42}O_2S_4$. The IR spectrum displayed characteristic bands at 3030, 1585, 860 (aromatic ring), 1705 (COOH), 1620 (C=C) and 965 cm^{-1} (C=C, *trans*). The NMR of this compound also supported its structure. It gave signals at δ 7.31 m (2H, C5-aromatic protons), 6.9 m (6H, C2- and C6-aromatic protons and two vinylic protons present between the two thiolane rings), 2.2 (12H, methylene protons α- to acid carbonyl and dithiolane rings merged in part with methyl protons of the toluene rings) along with other usual signals observed for fatty


CH3 - (CH2)5 - C - CH = CH - C - (CH2)7 - COOH
O O
(V)
SH
SH
CH3
BF3-etherate/AcOH
CH3 - (CH2)5 - C - CH = CH - C - (CH2)7 - COOH
S S S S
CH3 CH3

(XIII)

+


CH3 - (CH2)5 - C - CH = CH - C - (CH2)7 - COOH
O/R R/O
R =
S
S
CH3

(XIV)

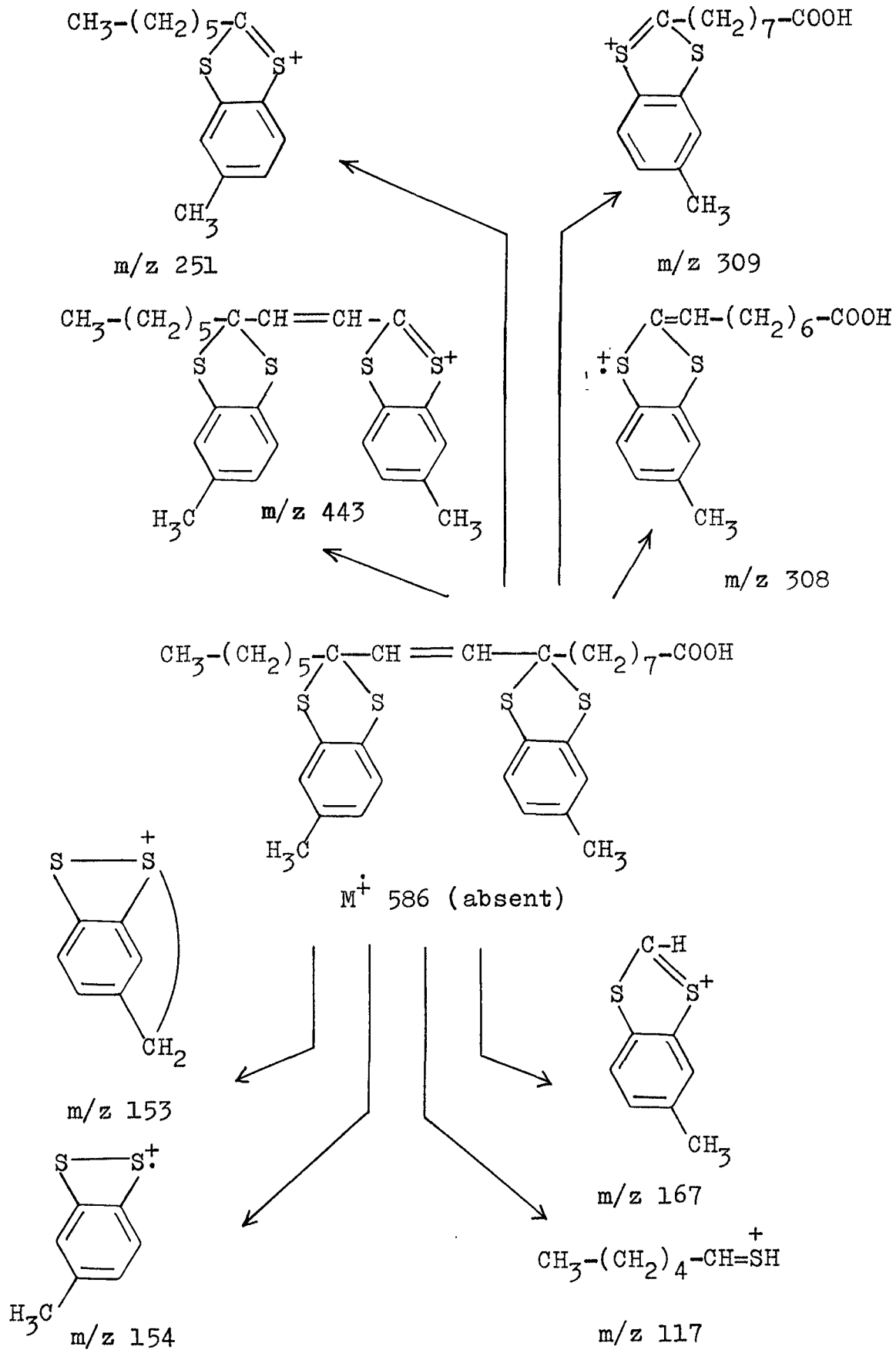
acids. These signals showed that double bond remained unaffected during the reaction and both the oxo groupings were condensed with the reagent. Thus the structure 9,9,12,12-bis-toluene-3,4-disulfideoctadec-trans-10-enoic acid was assigned to XIII.

The mass spectrum (Scheme 6, Fig. 7) had no molecular ion peak. The α-cleavages to the ring from the side of unsaturation are not prominent and gave peaks of very low intensity at m/z 309 and 251 due to the presence of double bond α- to the rings. The presence of fragment 443, arising due to the loss of $(CH_2)_7$-COOH from the molecular ion established that both the oxo groups have been condensed with the toluene-3,4-dithiol. Other significant mass ions, characteristic of dithiolane grouping appeared at 291 ($309-H_2O$), 276 ($291-CH_3$), 244 (276-S), 193, 181, 167, 156 (154+2H), 155 (154+H), 154, 153, 121, 119 (117+2H), 117 and 91. Thus MS data confirmed the structure of XIII.

Characterization of the Product (XIV)

This compound was analyzed for $C_{25}H_{36}O_3S_2$. The IR spectrum showed bands at 3030, 1590 and 860 cm^{-1} for aromatic ring. The diagnostic bands at 1690 and 960 were observed for α-β, unsaturated oxo function and trans double bond respectively. Other absorptions appeared at 1620 (C=C, olefin) and 1710 (COOH). Its NMR spectrum exhibited a broad multiplet signal at δ 7.4 for C5-aromatic proton and a four proton multiplet at 6.8 which was assigned to C2-and C6-aromatic protons merged

Scheme 6


m/z 251
m/z 309
m/z 443
m/z 308
M+ 586 (absent)
m/z 153
m/z 167
m/z 154
m/z 117

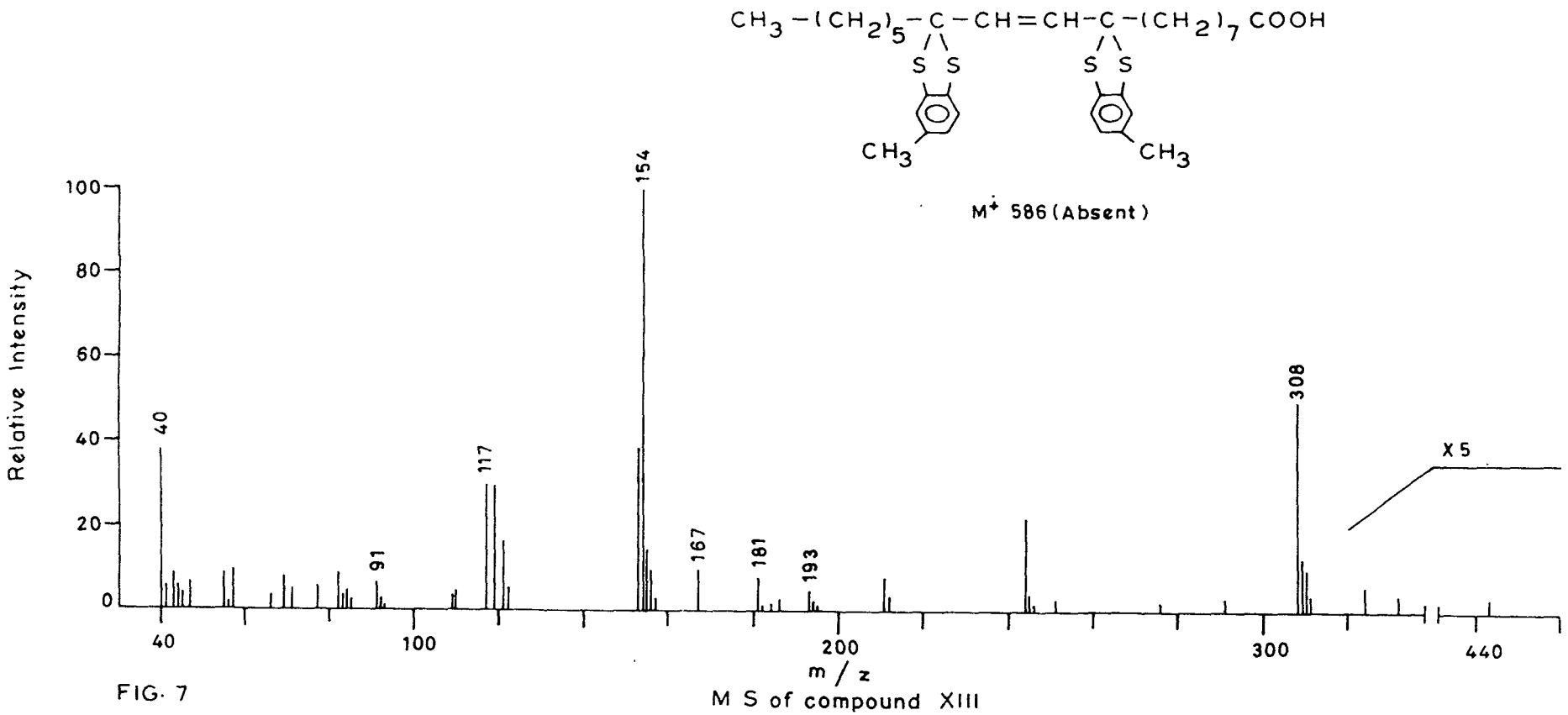


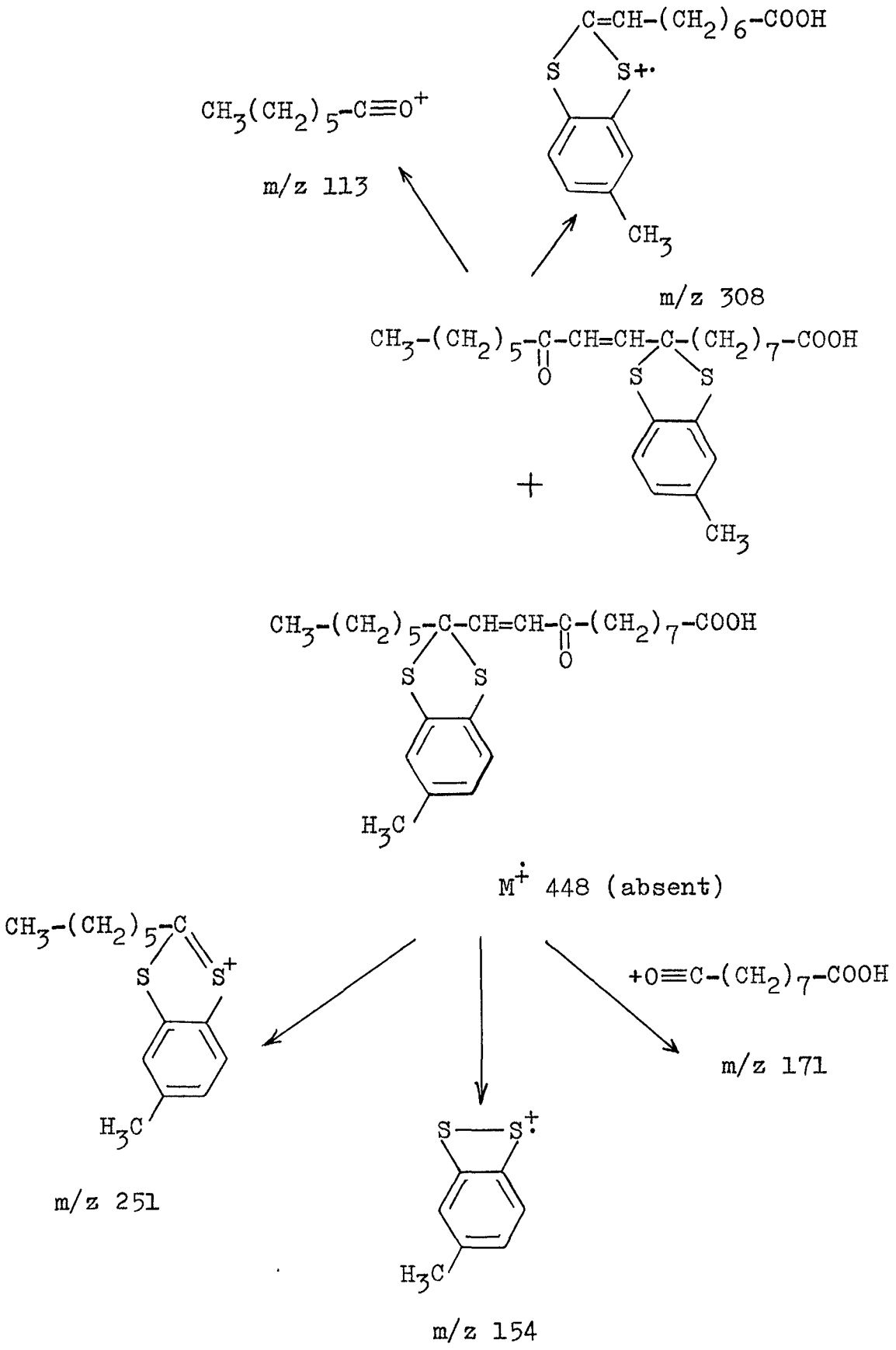
FIG. 7

M S of compound XIII

with olefinic protons. Another signal at 2.2 integrating for nine protons was attributed to methylene protons α-to oxo grouping and ring, merged in part with methyl protons of the toluene. Other usual signals were observed at 1.25 and 0.9. These spectral data suggested the structure of XIV as 9(12)-toluene-3,4-disulfide-12(9)-oxooctadec-trans-10-enoic acid.

Mass spectrum of XIV further confirmed this isomeric structure (Scheme 7, Fig. 8). Molecular ion peak at m/z 448 was nonexistent. The structure-revealing peaks present in its spectrum at 308, 251, 171 and 113 confirmed the isomeric nature of the product. Other significant mass ions and characteristic of dithiolane grouping were observed at 309 (308+H), 310 (308+2H), 294 (309-CH_3), 276 (308-S), 259(277-H_2O), 244 (259-CH_3), 221, 211, 167, 154, 149, 121 (154-SH), 119 (117+2H), 117, 105, 91, 71, 57, 43 and 40 (base peak).

Scheme 7


C=CH-(CH2)6-COOH
S
S+·
CH3(CH2)5-C≡O+
m/z 113
CH3
m/z 308
CH3-(CH2)5-C-CH=CH-C-(CH2)7-COOH
O
S
S
CH3
+
CH3-(CH2)5-C-CH=CH-C-(CH2)7-COOH
O
S
S
H3C
M+ 448 (absent)
CH3-(CH2)5-C
S
S+
H3C
m/z 251
+O≡C-(CH2)7-COOH
m/z 171
S
S+·
H3C
m/z 154

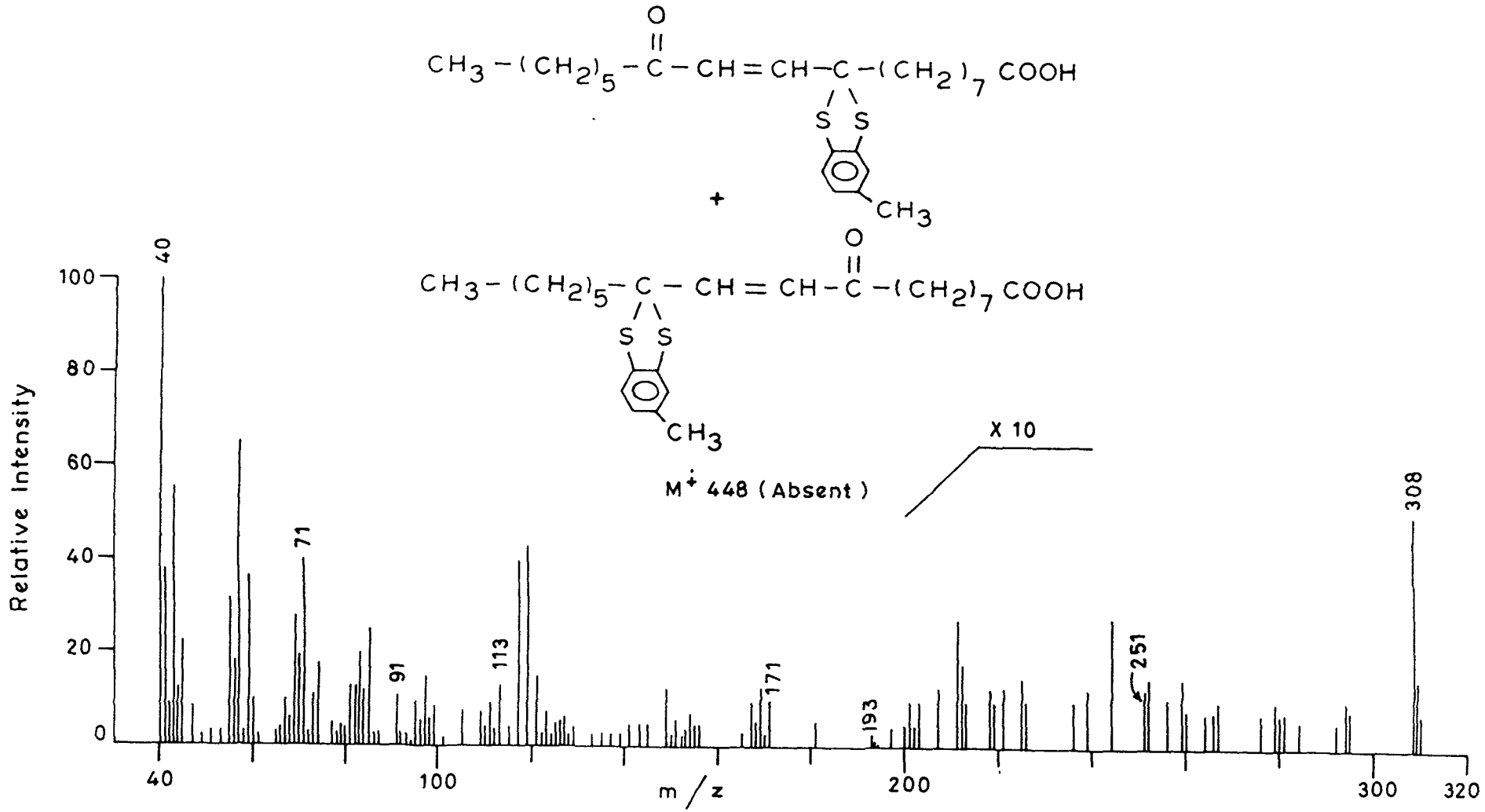


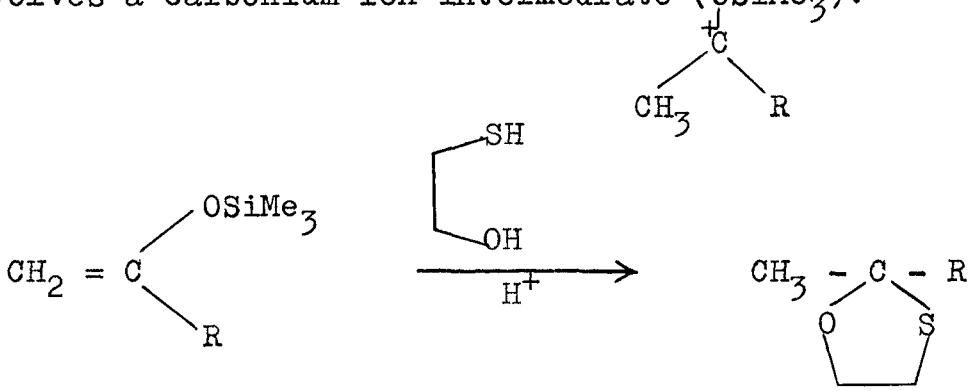
FIG. 8

M S of compound XIV

Chapter 4.2

Synthesis of Long Chain Oxathiolanes

Like dithiolanes, oxathiolanes have also been described as radio protectant[23]. In recent years oxathilanes have attracted attention due to their pharmaceutical utility[25] and antineoplastic activities[32]. Scanning of the literature revealed that ketones readily condensed with β-mercapto-ethanol in the presence of various catalysts[5-13] to furnish oxathiolanes. Recently Larson and Hernandez[33] have also reported a method for the synthesis of oxathiolanes. The procedure is a simple acid-catalyzed reaction of TMS (trimethylsilyl) enol ethers with β-mercaptoethanol, which involves a carbonium ion intermediate ($OSiMe_3$).

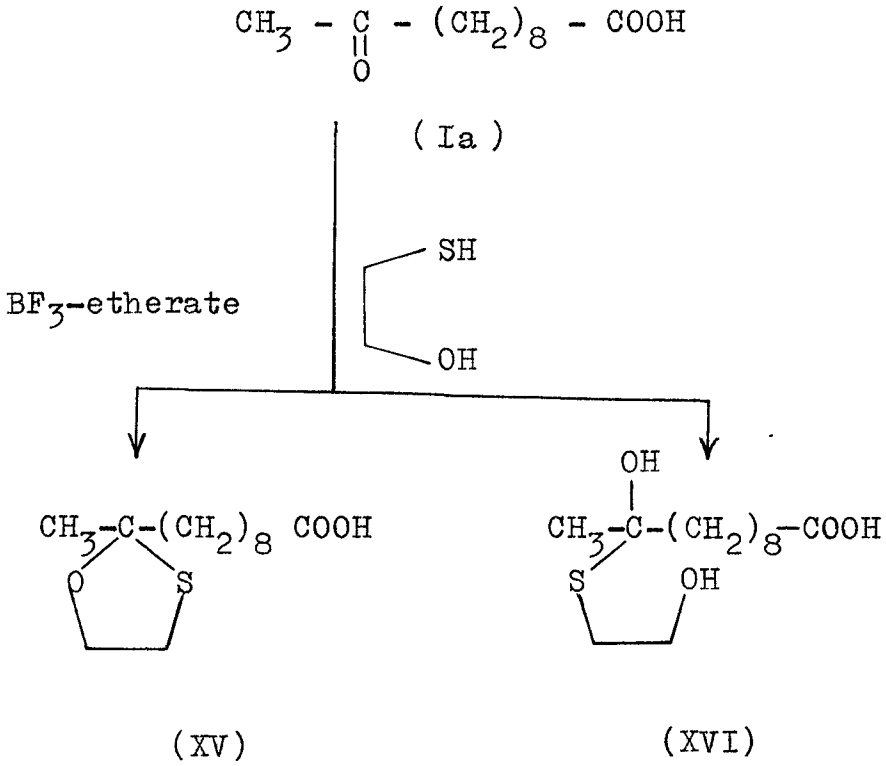


The resurgence of interest in oxathiolanes for their pharmacological activity and our derivatization program

for the synthesis of fatty heterocycles[15], led us to undertake the present work on the synthesis of long chain oxathiolanes from keto fatty acids. Earlier the same reaction was carried out with methyl 10-oxoundecanoate and methyl 12-oxooctadecanoate in presence of BF_3-etherate and acetic acid to give only oxathiolanes[34]. In the present study only BF_3-etherate (solvent as well as catalyst) was used for condensation of 10-oxoundecanoic and 9-oxooctadecanoic acids in order to isolate the intermediate, the corresponding hemimercaptals. In the case of methyl 9,10-dioxooctadecanoate, acetic acid was used to dissolve the dioxo ester and BF_3-etherate was added as catalyst. The mass fragmentation pattern of oxathiolanes was also studied.

Reaction of β-Mercaptoethanol with 10-Oxoundecanoic Acid (Ia)

10-Oxoundecanoic acid was allowed to react with β-mercaptoethanol in the presence of BF_3-etherate according to the procedure of Fieser[13]. After final work up and fractionation over silica gel column two TLC homogeneous products (XV as major and XVI as minor) were obtained.



(XV) (XVI)

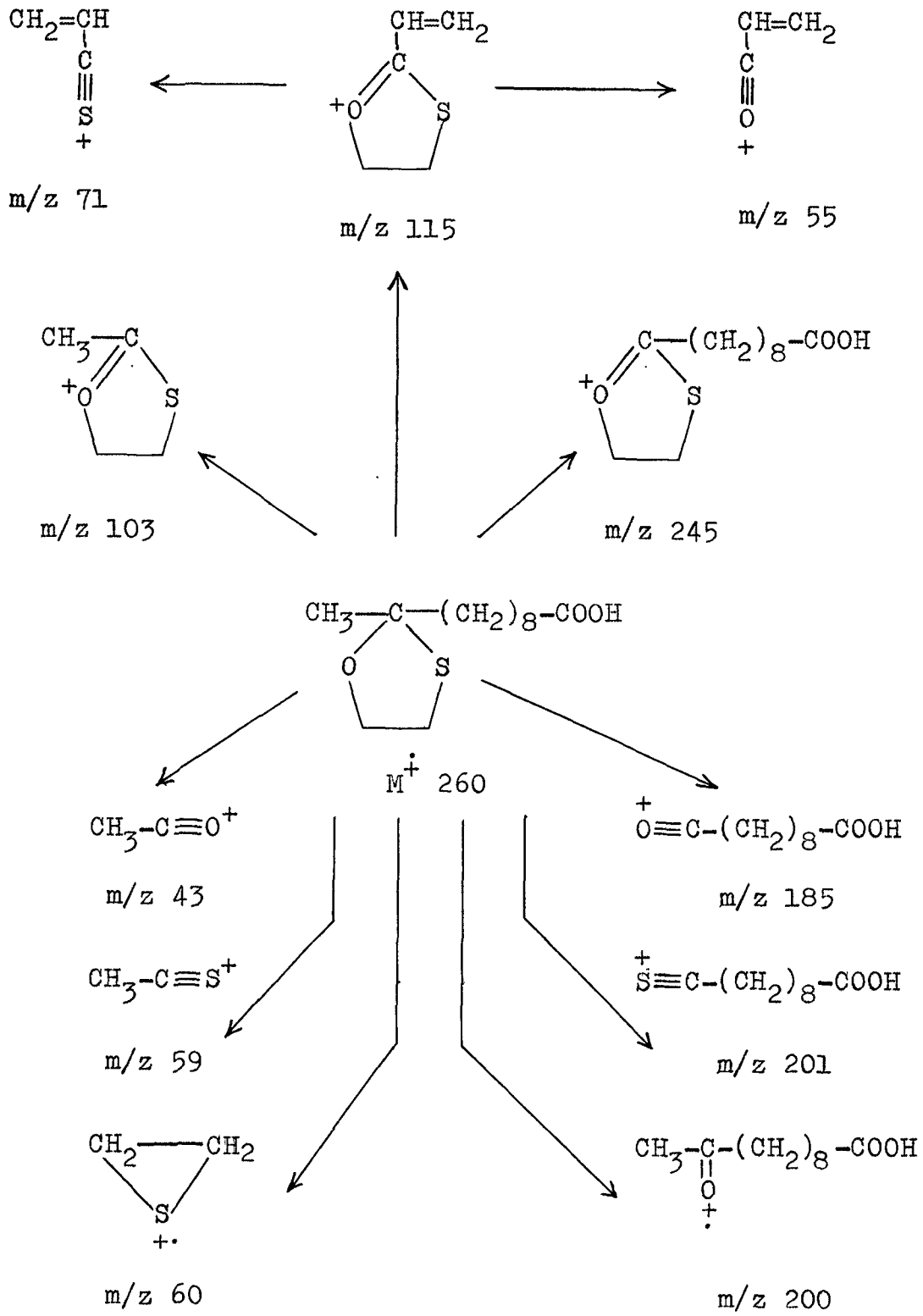
Characterization of the Major Product (XV)

Elemental analysis corresponded to formula $C_{13}H_{24}O_3S$. Its IR spectrum had a characteristic band at 1050 cm^{-1} for oxathiolane grouping[10] which is suggestive of the incorporation of oxathiolane ring in the fatty acid chain. In addition, two more bands appearing at 1435 (CH_2-S, deformation)[35,36] and 1250 (CH_2-S, wagging) indicated the presence of sulfur atom. The NMR spectrum of the compound exhibited signals at δ 4.15 and 2.85 as triplets and were attributable to methylene protons attached to oxygen and sulfur of the oxathiolane ring respectively. The downfield appearance of the

C9-methylene and terminal methyl protons at 1.7 and 1.5 respectively is due to the presence of oxathiolane ring at C10. The other usual signals appeared at 2.3 (methylene protons α-to acid carbonyl), 1.3 (chain methylene protons) and 9.1 (D_2O exchangeable acid proton). On the basis of spectral and combustion data the structure of the product (XV) was formulated as 10-(ethyleneoxathiolane) undecanoic acid.

The above structue was further supported by its mass spectrum (Scheme 8, Fig. 9). It gave highest ion peak at m/z 260 which corresponded to the molecular ion. The diagnostic fragments at 245 and 103 arising from the α-cleavages to ring. established the position and nature of the ring in the chain. The mass ions at 60 (ethylenesulfide) and 200 generating from molecular ion are due to the elimination of ethylenesulfide from the oxathiolane ring as described earlier[28]. A characteristic fragment ion of oxathiolane ring was observed at m/z 115. The genesis of this ion is the same as described for dithiolane ring in Chapter 4.1. In the lower mass ion range the peaks at 55 and 71 are deemed to emerge from secondary fragmentation of the mass ion 115[28]. Elimination of S, SH, H_2S and H_2O generally occurs from the molecular ion and from α-cleavage fragment ions, m/z 103, 245. The other ions at 83 (115-S, base peak), 81 (115-H_2S), and 97(115-H_2O) arise from the mass ion 115. The oxygen-containing fragments

Scheme 8


m/z 71
m/z 115
m/z 55
m/z 103
m/z 245
M+ 260
m/z 43
m/z 185
m/z 59
m/z 201
m/z 60
m/z 200

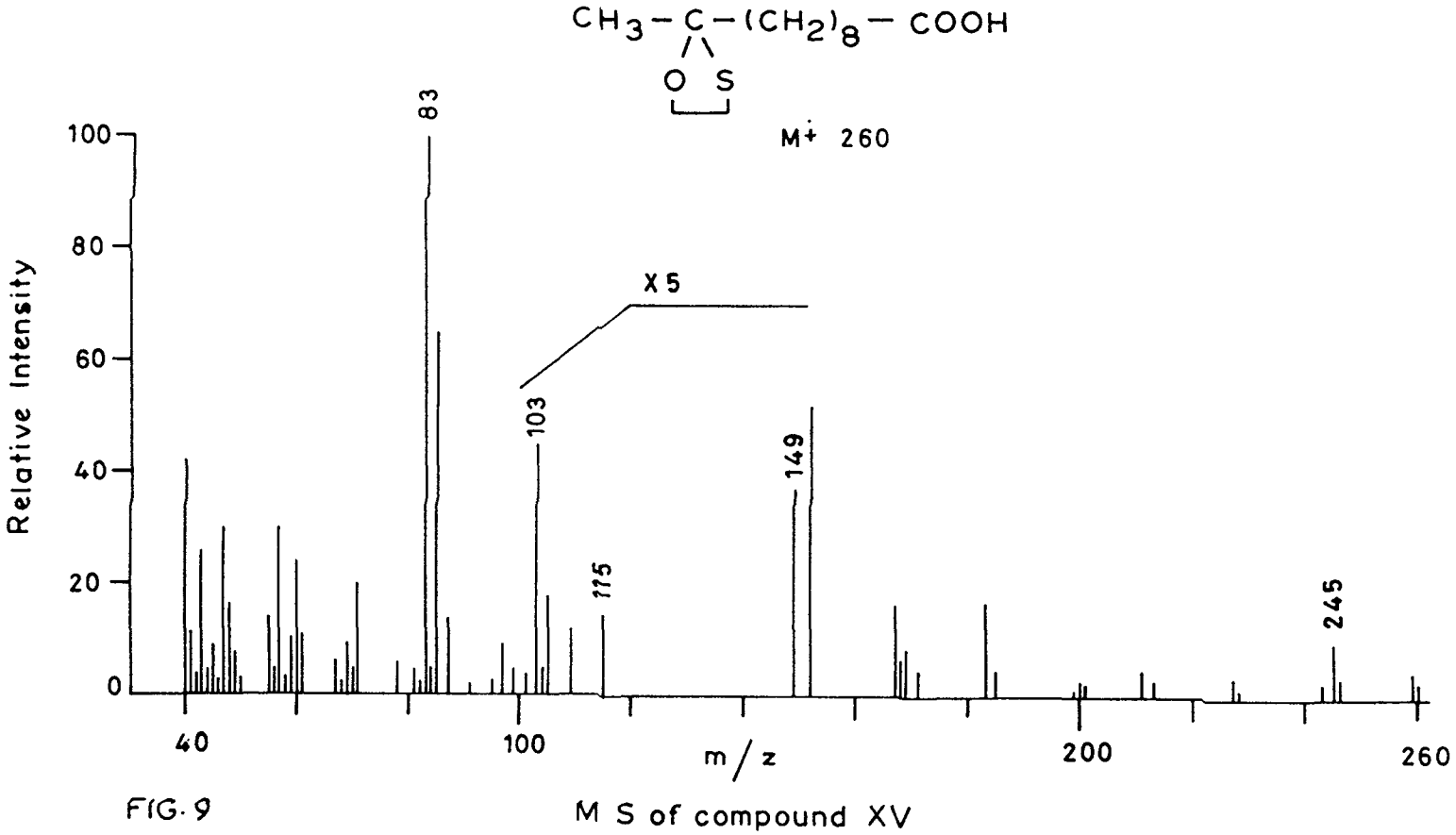


FIG. 9

M S of compound XV

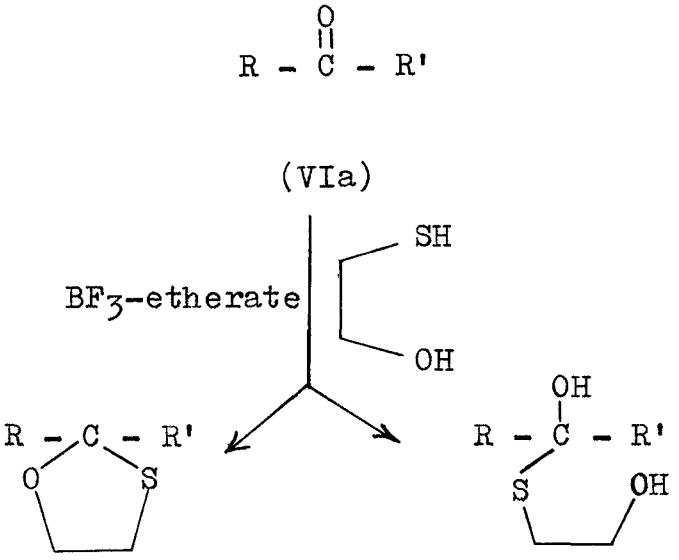
at 45, 59, 87, 101,..... due to long chain acid and alkyl fragments at 43, 57, 71, 85, 99,..... were also observed. Other salient mass ion peaks were observed at 259 (M-H), 246 (245+H), 243 (M-OH), 228 (245-OH), 227 (M-SH), 213 (246-SH), 211 (245-H_2S), 183 (201-H_2O), 169 (201-S), 168 (201-SH), 167 (201-H_2S or 185-H_2O), 152 (169-OH), 149 (167-H_2O) and 104 (103+H).

Characterization of the Minor Product (XVI)

The identity of the product (XVI) as 10-hydroxy-10-(2'-hydroxyethylmercapto)undecanoic acid was established on the basis of their chromatographic (highly polar), IR (3440 cm^{-1} for hydroxyl group) and NMR (D_2O exchangeable proton signal) behaviors. The isolation of the intermediate hemimercaptal may be explained due to lesser nucleophilicity of oxygen atom, which enables the complete conversion of hemimercaptal to oxathiolane. The elemental analysis of XVI corresponded to the formula $C_{13}H_{26}O_4S$. Its IR spectrum gave bands at 3440 (OH), 1715 (COOH), 1455 (CH_2-S, deformation) and 1260 cm^{-1} (CH_2-S, wagging). The NMR spectrum gave conclusive support in favor of the structure of XVI. It gave signals at δ 4.22 m (-CH_2-OH), 3.9-3.6 br m (2 x -OH, D_2O exchangeable), 2.85 t (-CH_2-S), 2.35 m (-CH_2-COOH), 1.7 m (C9-methylene protons α-to tertiary carbon), 1.55 s (terminal methyl protons α-to tertiary carbon) and 1.25 br s (chain-CH_2-).

Reaction of β-Mercaptoethanol with 9-Oxooctadecanoic Acid (VIa)

The reaction of β-mercaptoethanol with 9-oxooctadecanoic acid was carried out under the reaction conditions described earlier. TLC examination of the final reaction mixture revealed two distinct spots. The fractionation gave XVII as major and XVIII as minor products.



(XVII) (XVIII)

R = CH_3-$(CH_2)_8$

R' = $(CH_2)_7COOH$

Characterization of the Major Product (XVII)

The elemental analysis of the product (XVII) corresponded to formula $C_{20}H_{38}O_3S$. Its IR spectrum showed characteristic absorptions at 1705 (COOH), 1440 (CH_2-S, deformation), 1255 (CH_2-S, wagging) and 1045 cm^{-1} (oxathiolane ring). The

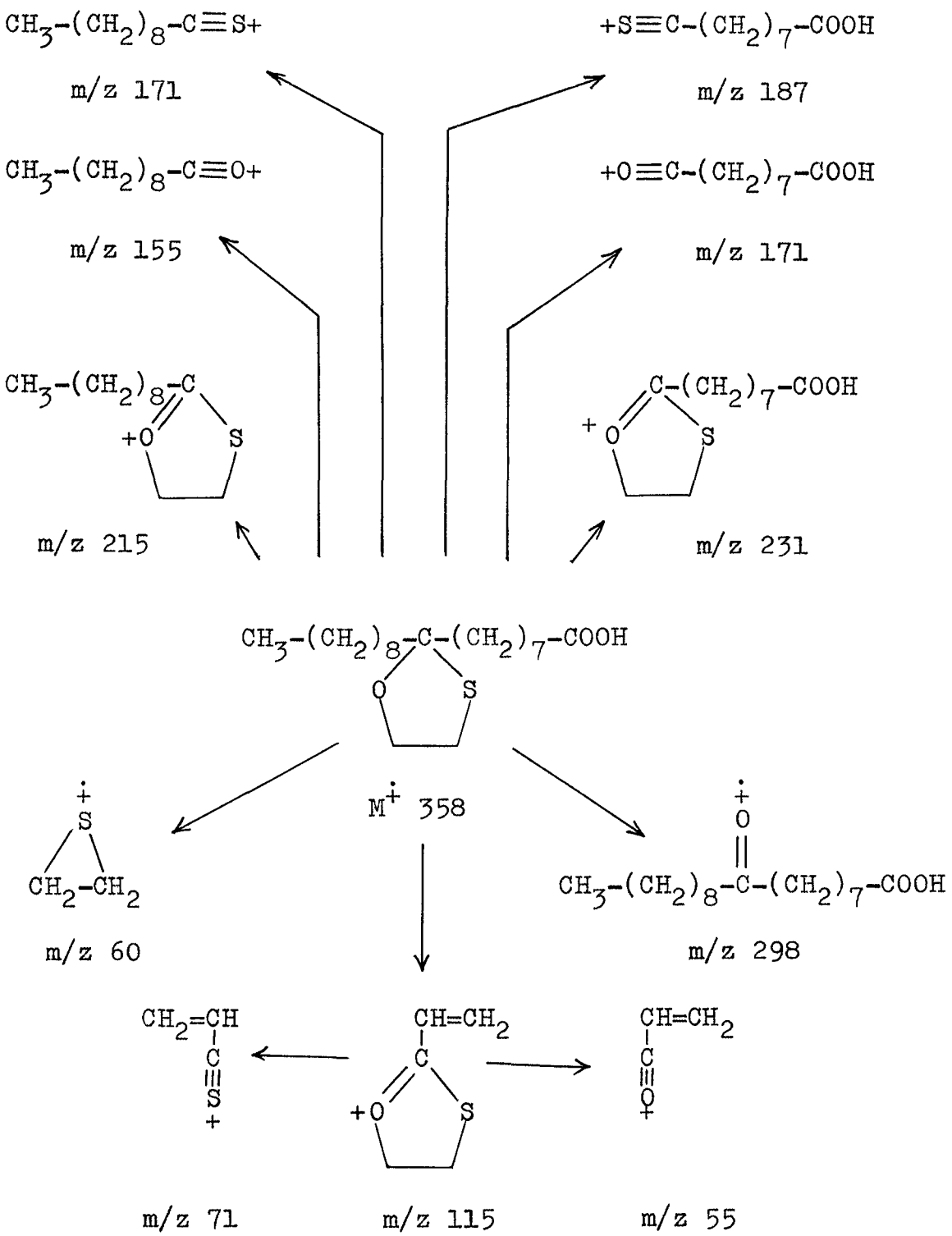
NMR spectrum exhibited signals at δ 4.15 t ($-C\underline{H}_2-O$, of ring), 2.8 t ($-C\underline{H}_2-S$, of ring) and a multiplet at 1.7 for four protons (2 x $-C\underline{H}_2-$) α- to the oxathiolane ring. The other usual fatty signals were observed at 2.28 m ($-C\underline{H}_2COOH$), 1.32 br s (chain methylene protons) and 0.85 t (terminal methyl protons). On the basis of these spectral data the product (XVII) was characterized as 9-(ethyleneoxathiolane) octadecanoic acid.

Its mass spectrum (Scheme 9, Fig. 10) gave very small molecular ion peak at m/z 358, followed by other diagnostic peaks at 231 and 215 arising from the α-cleavage to the oxathiolane ring. Two other significant peaks at 60 and 298 were observed due to the loss of ethylenesulfide (m/z 60) from the molecule. Other diagnostic peaks at 115 (characteristic of oxathiolane)[28] and 97 (115-H_2O), 83 (115-S), 81 (115-H_2S), 71 and 55 emerging from the mass ion 115 were also recorded. Some other prominent ion peaks were also observed at 357 (M-H), 341 (M-OH), 325 (M-SH), 298 (M-60), 281 (298-OH), 233 (231+2H), 232 (231+H), 217 (215+2H), 216 (215+H), 199 (232-SH), 186 (231-45), 183 (216-SH), 201 (231-CH_2O), 187, 171, 167 (201-H_2S), 155, 149 (167-H_2O) and 43.

Characterization of the Minor Product (XVIII)

The compound XVIII gave satisfactory elemental analysis for $C_{20}H_{40}O_4S$. The IR spectrum displayed characteristic bands

Scheme 9


CH3-(CH2)8-C≡S+
m/z 171
+S≡C-(CH2)7-COOH
m/z 187
CH3-(CH2)8-C≡O+
m/z 155
+O≡C-(CH2)7-COOH
m/z 171
m/z 215
m/z 231
M+ 358
m/z 60
m/z 298
m/z 71
m/z 115
m/z 55

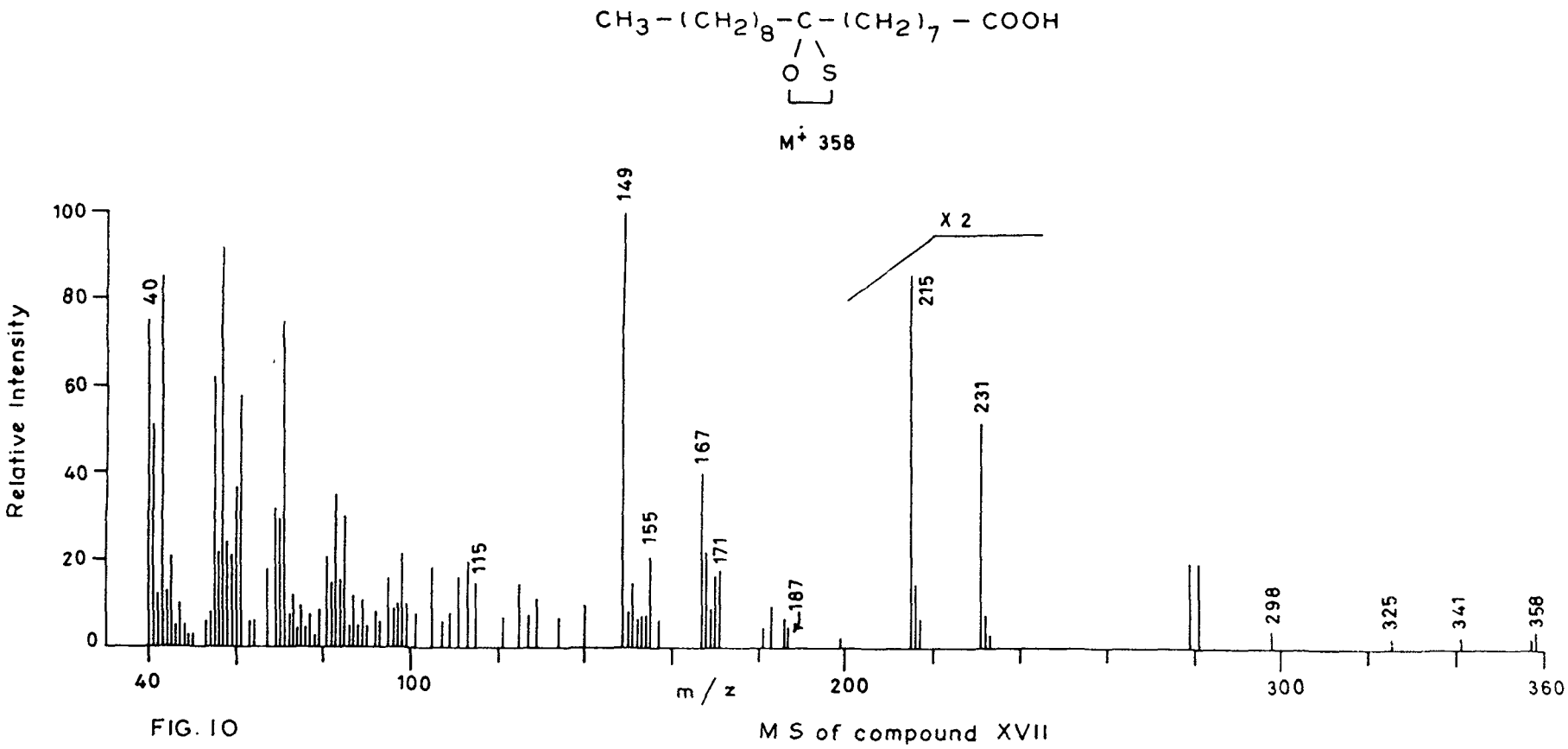


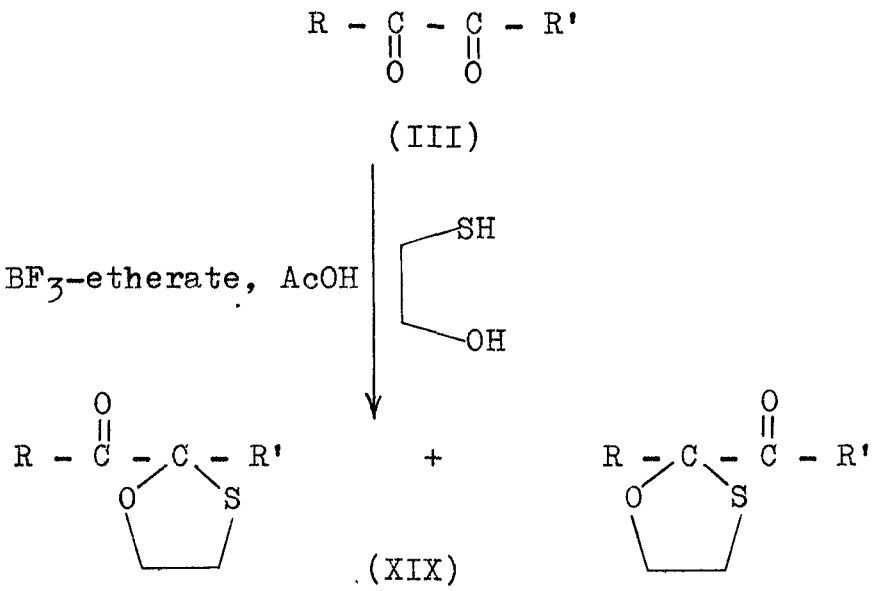
FIG. 10

M S of compound XVII

at 3490 (OH), 1710 (COOH), 1445 (CH_2-S, defor.) and 1250 (CH_2-S, wag.) which established the formation of hemimercaptal as in the previous case. The NMR spectrum displayed a diagnostic multiplet signal at δ 1.7 integrating for four protons attributable to the C8-and C10-methylene protons adjacent to the tertiary carbon atom. Another broad signal at 2.6 integrating for two protons was due to the two hydroxyl groups (D_2O exchangeable). Other characteristic signals appeared at 4.24 m (-CH_2OH), 2.8 t (-CH_2-S) along with the usual signals at 2.3 m (-CH_2COOH), 1.3 br s (chain-CH_2-) and 0.9 t (terminal -CH_3). These observations were consistent with the structure of this hemimercaptal as 9-hydroxy-9-(2'-hydroxyethylmercapto)octadecanoic acid.

Reaction of β-Mercaptoethanol with Methyl 9,10-dioxooctadecanoate (III)

The dioxo ester (III) was first dissolved in acetic acid and then allowed to react with β-mercaptoethanol in the similar fashion as described earlier. Usual work up and purification by column chromatography yielded an oily product (XIX).



$R = CH_3 - (CH_2)_7$ and $R' = (CH_2)_7\ COOCH_3$

Characterization of the Product (XIX)

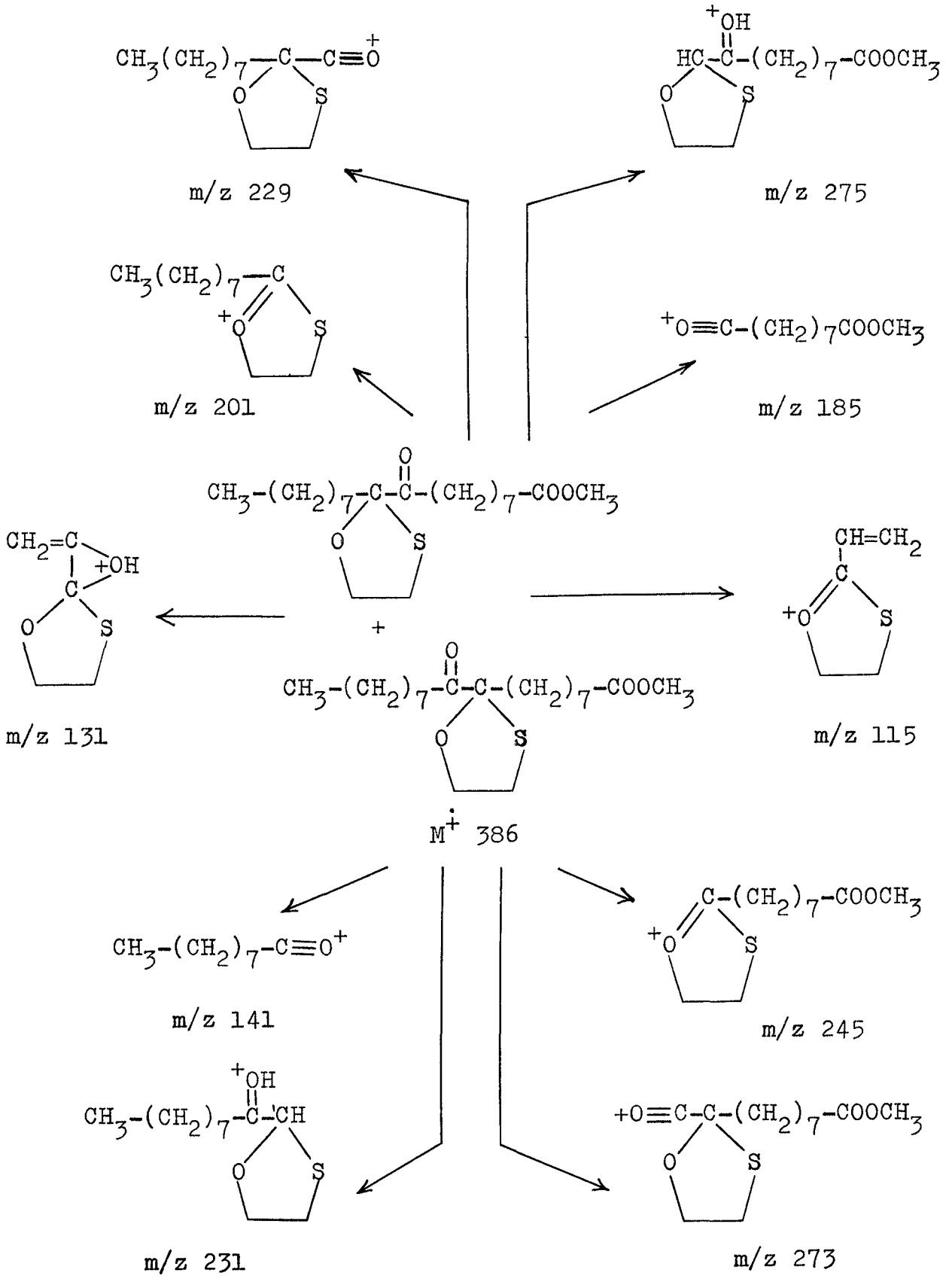
The microanalysis of XIX corresponded to the formula $C_{21}H_{38}O_4S$. Its IR spectral bands at 1435, 1230 and 1025 cm^{-1} suggested the presence of oxathiolane ring in the molecule. It further showed an absorption at 1715 which confirmed that one of the two carbonyl functions remained intact. The structure was further supported by its NMR spectrum. It had signals for the oxathiolane ring which appeared at δ 4.12 t and 2.72 t each integrating for two protons attached to oxygen and sulfur respectively. A multiplet at 2.3 counted for four protons can be attributed to methylene protons α-to ester and free carbonyl group. A characteristic signal at 1.65 appeared due to the methylene protons adjacent to the

oxathiolane ring. The other usual signals appeared at 3.6 s, 1.3 br s and 0.9 t. On the basis of these IR and NMR data the product (XIX) was characterized as an isomeric mixture of methyl 9(10)-(ethyleneoxathiolane)-10(9)-oxooctadecanoate.

The structure as well as the isomeric nature of the product (XIX) was substantiated by mass spectral fragmentation pattern (Scheme 10, Fig. 11). It showed molecular ion peak at m/z 386. Fragments at 245 and 201 resulted from the α-cleavages to the oxathiolane ring. Other characteristic mass ions which reveal the isomeric nature of the compound were at 275, 273, 231 and 229 (Scheme 10). Loss of H_2O, H_2S, OH and SH also occurred from the molecular ion peak or through fragments generated from α-cleavages, which resulted peaks at 369 (M-OH), 355 (M-SH or OCH_3), 227 (245-H_2O), 211 (245-H_2S), 183 (201-H_2O) and 167 (201-H_2S). The presence of mass ions at 115 and the secondary decomposition peaks at 71 and 55 further confirmed the presence of oxathiolane ring. Other salient peaks were at 327 (M-$COOCH_3$), 342 (M-$[CH_2]_2O$), 261, (275-CH_2), 243(275-S), 229 (273-$[CH_2]_2O$), 217 (231-CH_2), 213 (273-$[CH_2]_2S$), 185 (229-$[CH_2]_2O$ or 245-$[CH_2]_2S$), 171 (201-CH_2O), 169 (229-$[CH_2]_2S$), 141 (201-$[CH_2]_2S$), 131, and lower mass ions at 97 (115-H_2O), 83 (115-S), 81 (115-H_2S), 60 (ethylenesulfide) and 43.

By using only BF_3-etherate as a condensing agent, it was possible to isolate the intermediate hemimercaptals in small quantities besides the oxathiolane derivatives. In the

Scheme 10


m/z 229
m/z 275
m/z 201
m/z 185
m/z 131
m/z 115
M+ 386
m/z 141
m/z 245
m/z 231
m/z 273

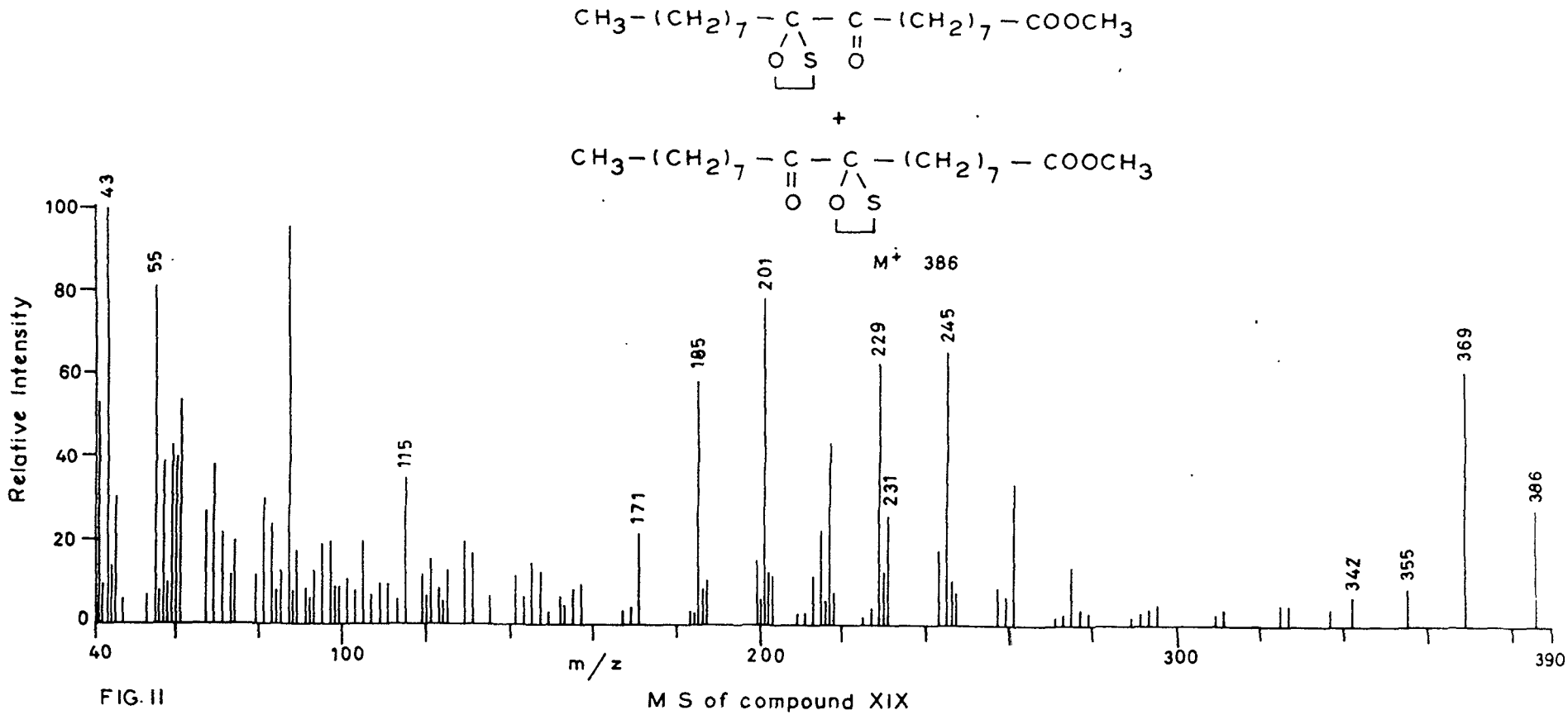


FIG. II

M S of compound XIX

earlier work[34], reaction of methyl 10-oxoundecanoate and methyl 12-oxooctadecanoate with β-mercaptoethanol in the presence of BF_3-etherate and acetic acid gave only oxathiolanes. This observation was further proved here in the reaction of methyl 9,10-dioxooctadecanoate with β-mercaptoethanol in presence of BF_3-etherate and acetic acid. It is expected that in the presence of acetic acid, the intermediate hemimercaptal cyclizes quickly to give the corresponding oxathiolane.

Chapter 4.3

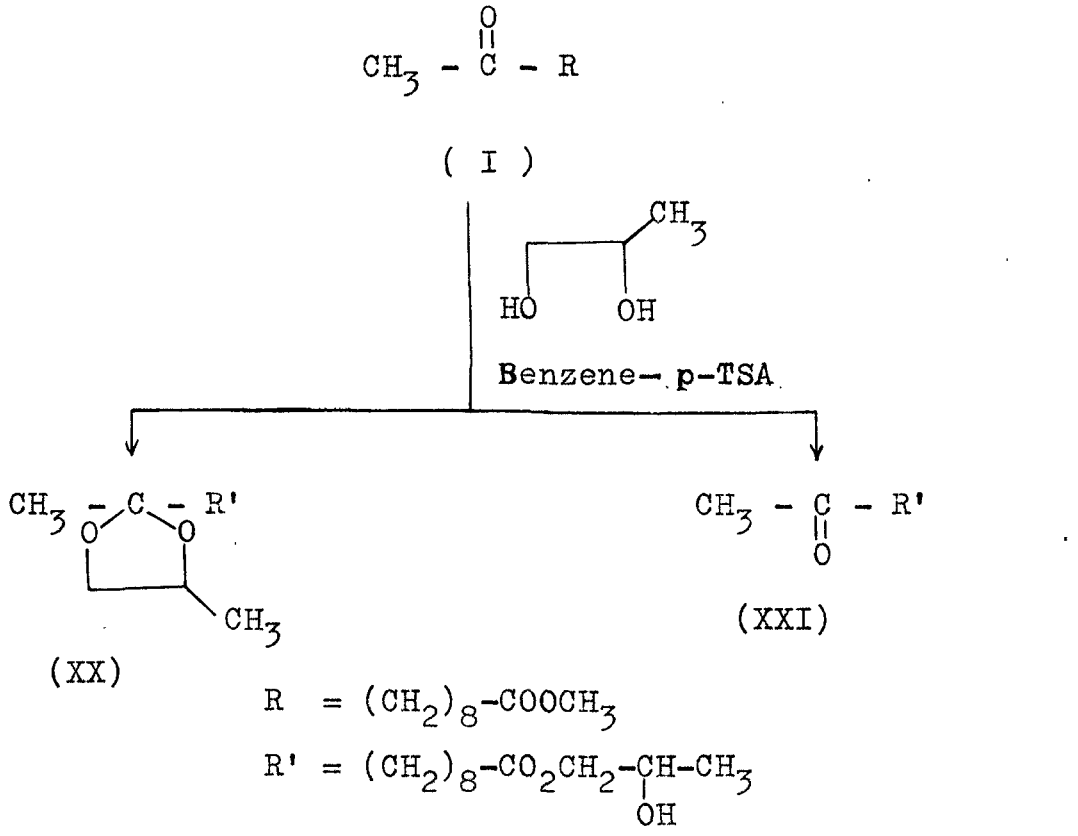
Synthesis of Long Chain Dioxolanes

Dioxolanation has been used both as a method for the protection of oxo function[12] and for the preparation of a variety of compounds showing industrial[32] and pharmaceutical potential[25]. Recently a number of dioxolanes have been identified as insecticides, fungicides and germicides[37-39]. A few dioxolanes have been used as flavoring materials[40] and also in perfumes[41]. However, there is very scanty literature on dioxolanes of fatty compounds, except one report from our laboratory[42]. In continuation of our work on derivatization of fatty acids[15] and keeping in the view the aforementioned importance of dioxolanes an attempt was made to synthesize methyl substituted dioxolanes from long chain oxo esters, using 1,2-propanediol, p-TSA and benzene as reagent, catalyst and solvent respectively.

Reaction of 1,2-Propanediol with Methyl 10-oxoundecanoate(I)

The reaction of excess of 1,2-propanediol with methyl 10-oxoundecanoate in a Dean Stark's apparatus was carried out in the presence of p-toluenesulfonic acid (p-TSA) according

to the procedure described by Williams et al.[43]. The reaction mixture after 2 hr reflux showed the complete conversion of the reactant on the TLC plate. After final work up, two TLC homogeneous products (XX) and (XXI) were obtained.



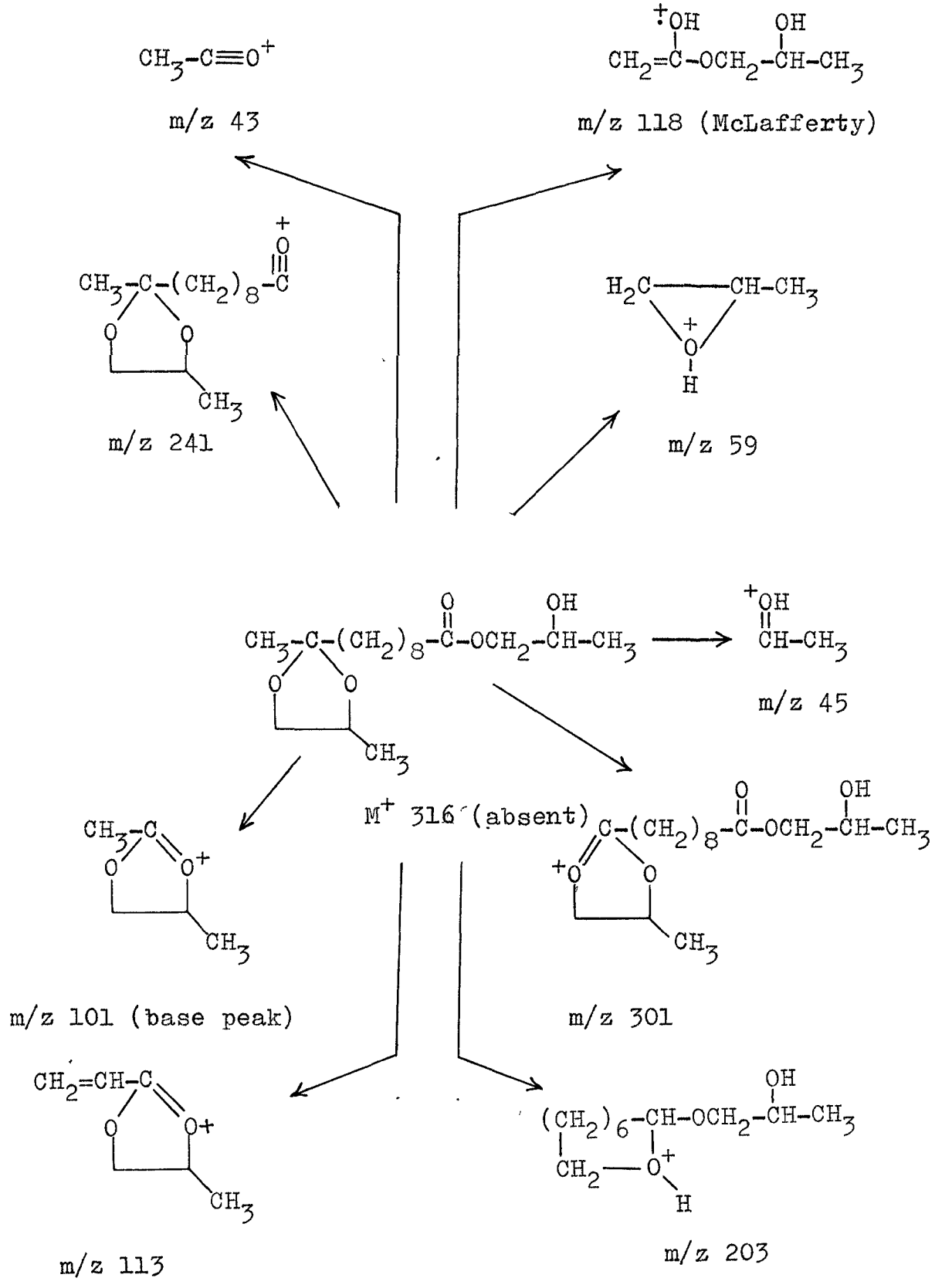
Characterization of the Major Product (XX)

The product (XX) gave satisfactory elemental analysis for $C_{17}H_{32}O_5$. Its IR spectrum had no band for the isolated oxo function. The characteristic bands at 1170, 1100 and 1050 cm^{-1} showed the incorporation of dioxolane ring[44] in the molecule. The ester carbonyl absorption appeared at 1740. Appearance

of a band at 3470 indicated the presence of hydroxyl group in the molecule. This may be attributed to the replacement of the methoxy group by 2'-hydroxypropoxy group. However, NMR spectrum was more informative and gave direct evidence of replacement of methoxy by 2'-hydroxypropoxy group. It had two multiplets centred at δ 3.95 and 3.5 for C1'-, C1"-methylene (2 x $-C\underline{H}_2-$) and C2'-, C2"-methine (2 x $-C\underline{H}-$) protons respectively. The signal at 2.75 br m (D_2O exchangeable) also suggested the presence of hydroxyl group in the compound. The spectrum of the compound was deprived of the strong methyl ester signal at 3.6. The downfield appearance of methylene protons in respect to methine protons of the ring and hydroxypropyl group was suggestive of the shielding nature of the methyl group directly attached to a secondary carbon atom. Terminal methyl and methylene protons α-to the dioxolane ring were merged with the broad singlet of the chain methylene protons at 1.23. Methylene protons α-to the ester carbonyl appeared at 2.25. The methyl protons of the ring and 2'-hydroxypropoxy group appeared at 1.15 as multiplet and partly merged with chain methylene protons. On the basis of the above data the product (XX) was characterized as 2'-hydroxypropyl-10-(2"-methylethylenedioxolane)undecanoate.

Mass spectrum of the compound (XX) (Scheme 11, Fig. 12) showed the parent ion at m/z 301 ($M-CH_3$). The characteristic mass ions at 301 and 101 arising from α-cleavages to the

Scheme 11


m/z 43
m/z 118 (McLafferty)
m/z 241
m/z 59
m/z 45
M+ 316 (absent)
m/z 101 (base peak)
m/z 301
m/z 113
m/z 203

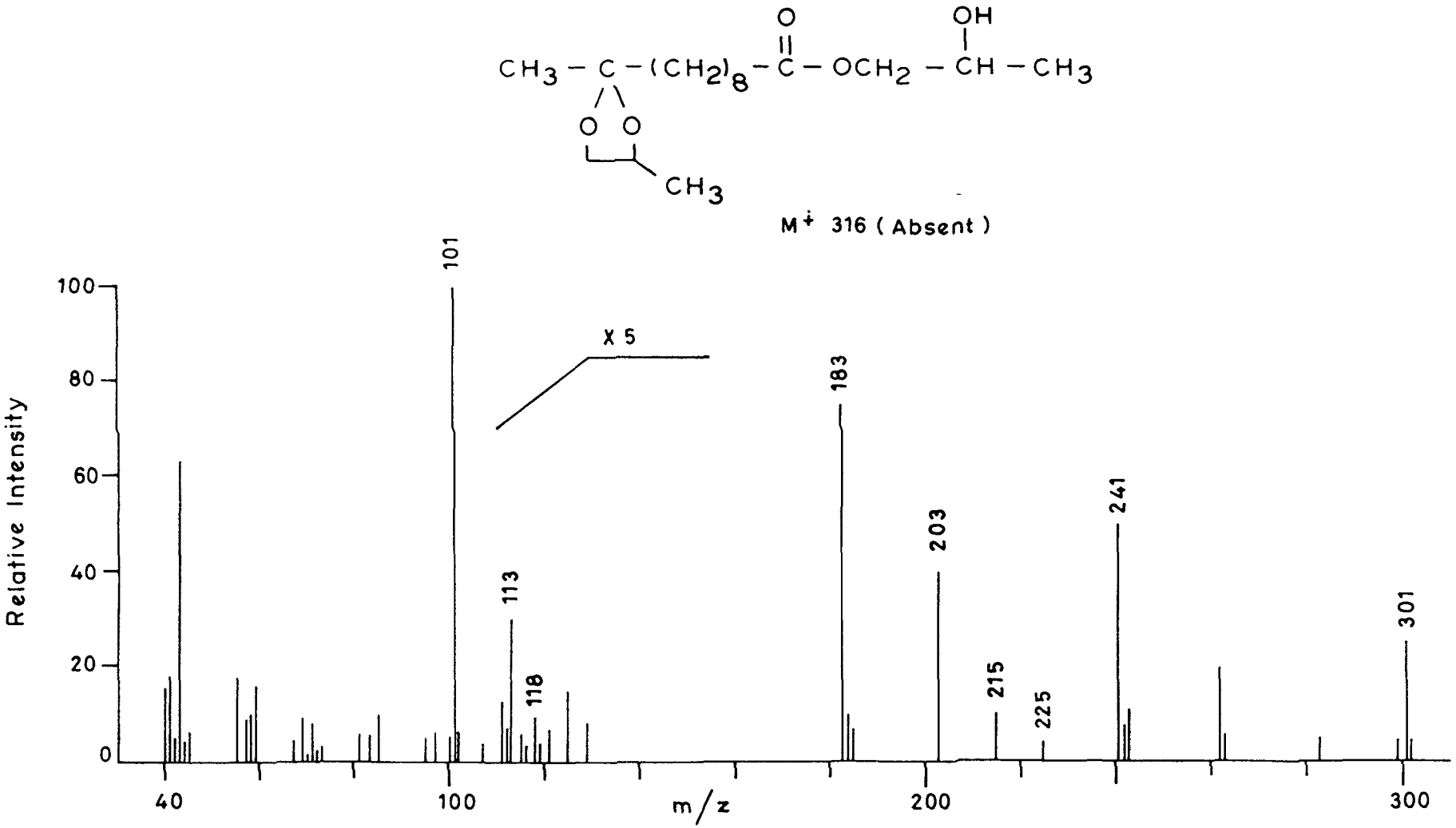


FIG. 12

M S of compound XX

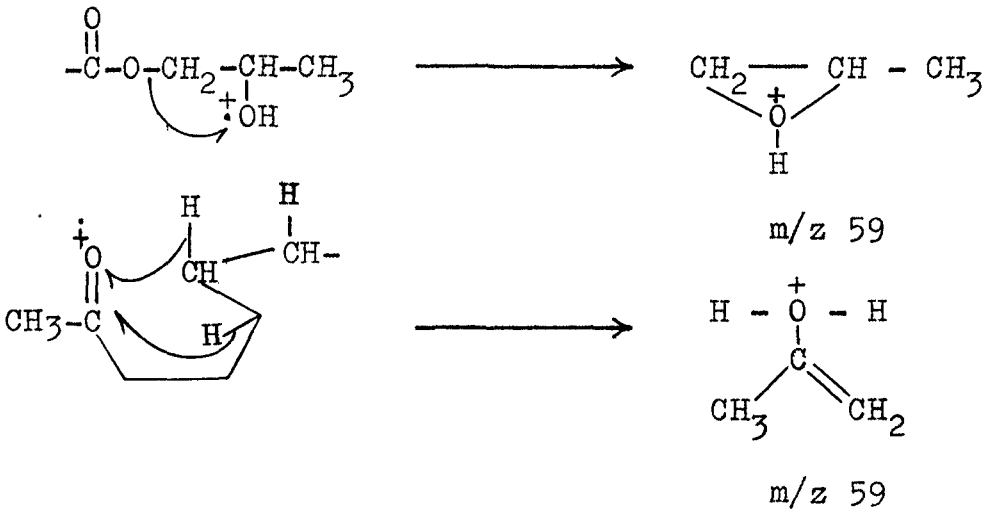
ring established the structure and position of the ring at C10. Other diagnostic mass ions were observed at 241, 118 (McLafferty), 113 and 43. The mass ion at 113 was considered as a characteristic of the dioxolane ring[28]. The genesis of the fragement ion at 113 required α-cleavage on one side and γ-cleavage on another side of the dioxolane group, accompanied by hydrogen transfer as described for dithiolanes in Chapter 4.1. Other salient peaks were present at 302(301+H),299 (M-OH), 283 (301-H_2O), 262, 243 (301-C_3H_6O), 241, 225 (243-H_2O), 215 (M-101), 203, 183 (241-C_3H_6O), 102 (101+H), 100(118-H_2O), 95 (113-H_2O), 83 (101-OH) and lower mass ions at 59,55(113-C_3H_6O), 45 and 43 ($CH_3C{\equiv}O^+$).

Characterization of the Minor Product (XXI)

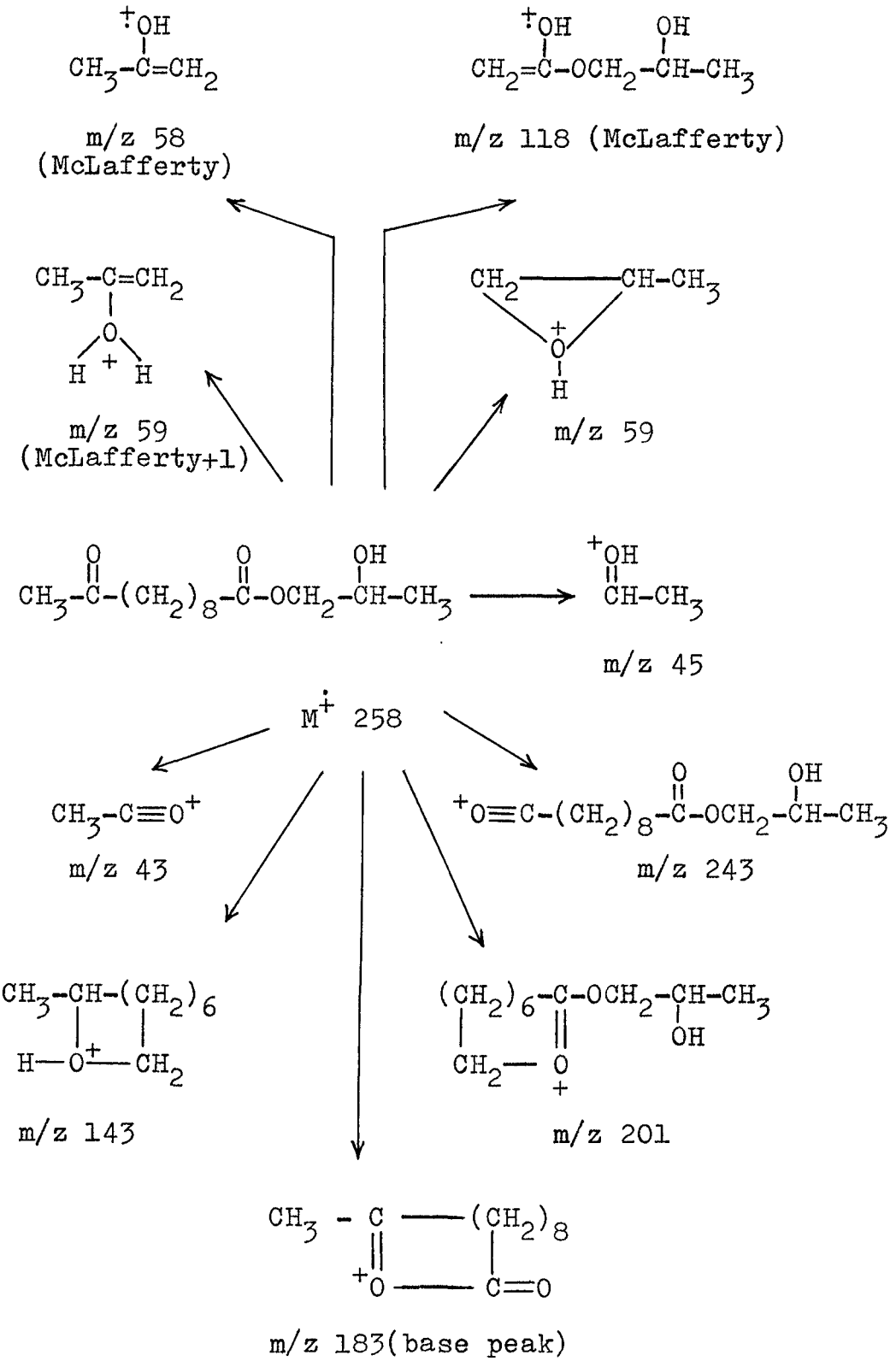
The combustion data of the compound (XXI) was equivalent to formula $C_{14}H_{26}O_4$. Its IR spectrum showed band at 1695 cm^{-1}, which indicated that the oxo function was intact in the molecule. A strong band at 3440 was attributable to hydroxyl function present in the molecule. The replacement of methoxy group by 2'-hydroxypropoxy group was confirmed by its NMR spectrum. It showed a doublet integrating for two protons at δ 3.9 and one proton multiplet at 3.55 for methylene and methine protons of the 2'-hydroxypropyl group respectively. A three proton sharp singlet at 2.08 was indicative of the unreacted oxo function. A signal at 2.35 integrating for

four protons attributable to C2- and C9-methylene protons α-to ester carbonyl and oxo group. Methyl protons of hydroxypropyl group observed at 1.15 as a doublet, merged in part with chain methylene protons at 1.3. A broad multiplet signal at 2.55, which disappeared after D_2O shake was due to the hydroxyl group of the molecule. These data suggested the structure of XXI as 2'-hydroxypropyl-10-oxoundecanoate.

MS of XXI had the molecular ion at m/z 258. The significant peaks (Scheme 12, Fig. 13) were observed at 259 (M+H), 241 (M-OH), 243 ($M-CH_3$), 240 ($M-H_2O$), 183 (base peak), 118, 59 and 58 (McLafferty). The greater abundance of fragment ion 59 in this case as compared to earlier observation suggested that this fragment ion originates due to 2'-hydroxy-propyl group as well as due to "McLafferty + 1" rearrangement of the free carbonyl group. This type of rearrangement was earlier observed in long chain ketones[45]. These characteristic peaks corroborated the above structure. Other salient mass ions were observed at 201 (β-cleavage), 184 (201-OH), 143, 125 ($143-H_2O$), 101 (118-OH), 45 and 43 ($CH_3C\equiv O^+$).



Scheme 12


m/z 58 (McLafferty)
m/z 118 (McLafferty)
m/z 59 (McLafferty+1)
m/z 59
m/z 45
M+ 258
m/z 43
m/z 243
m/z 143
m/z 201
m/z 183(base peak)

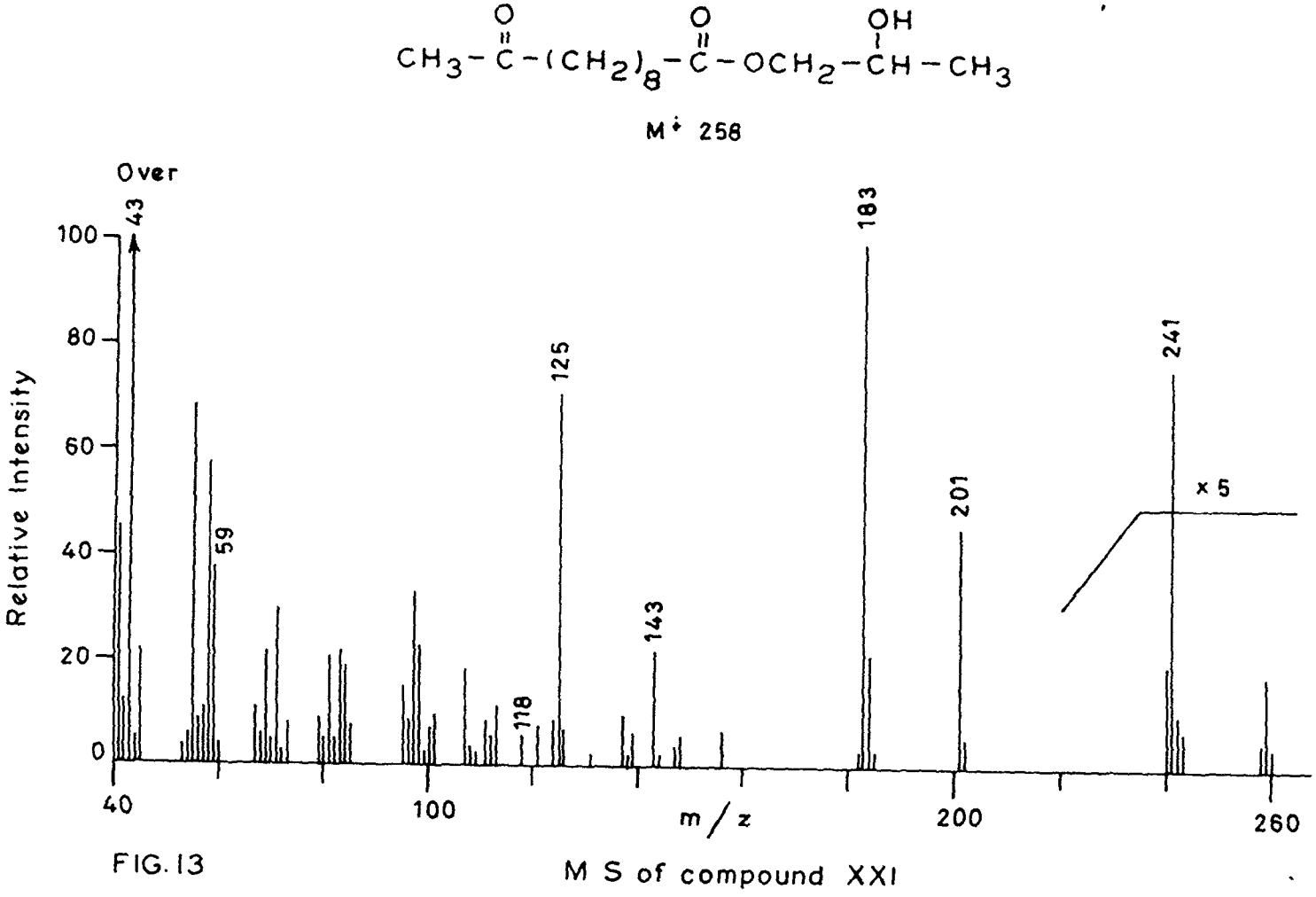
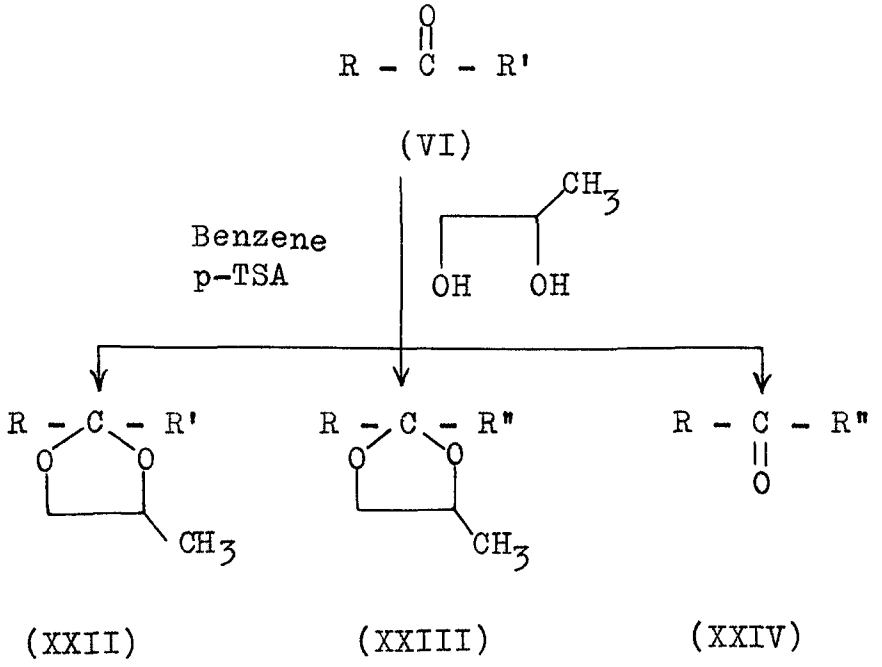


FIG. 13

M S of compound XXI

Reaction of 1,2-Propanediol with Methyl 9-oxooctadecanoate (VI)

This oxo ester (VI) on treatment with excess of 1,2-propanediol and traces of p-TSA yielded three TLC homogeneous products. Fractionation over silica gel column afforded two liquid products (XXII and XXIII) and one solid product(mp. 76-77 C, XXIV).



(XXII) (XXIII) (XXIV)

R = CH_3-$(CH_2)_8$; R' = $(CH_2)_7$-$COOCH_3$;

R" = $(CH_2)_7$-$COOCH_2$-$CH(OH)CH_3$

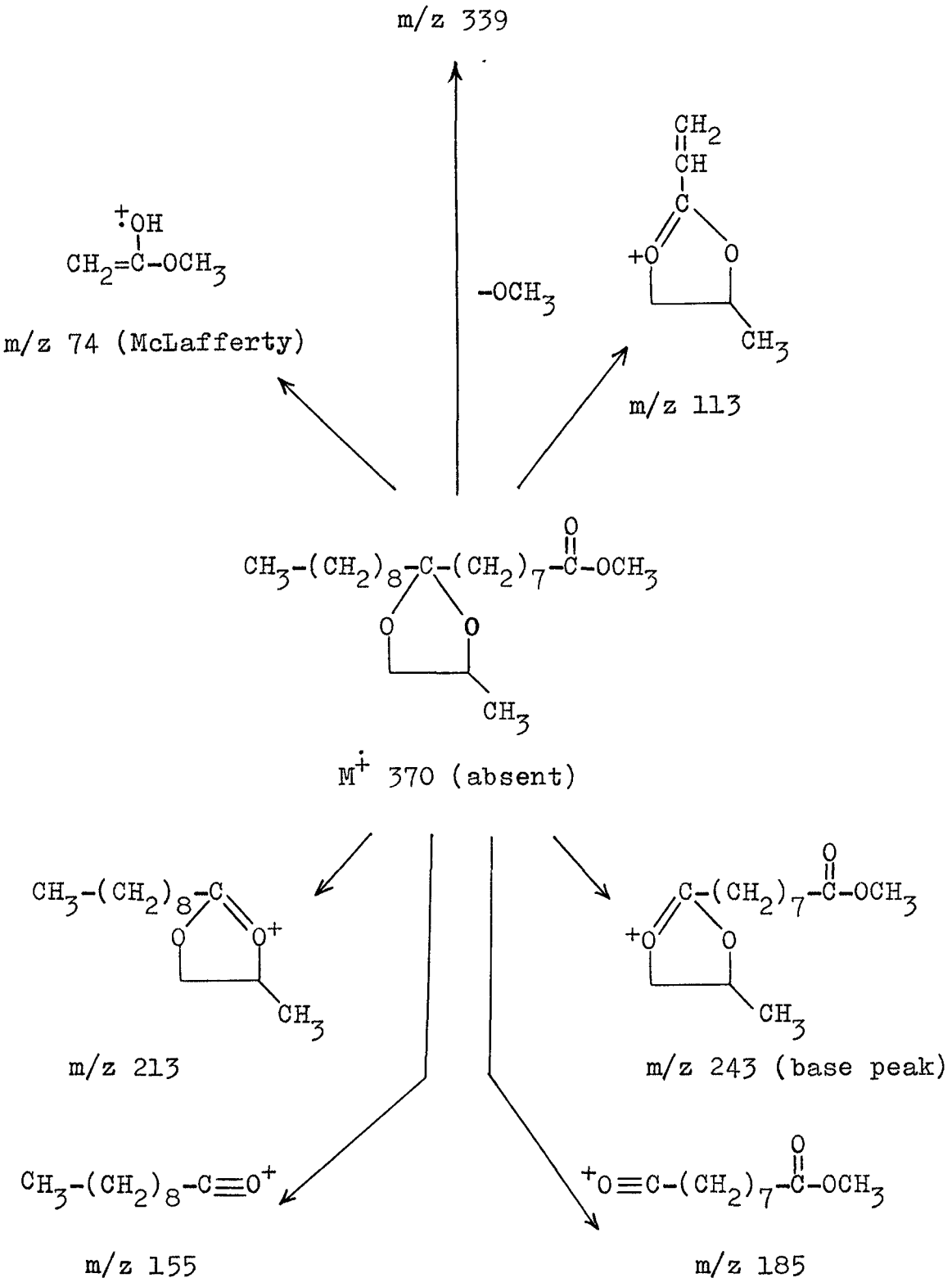
Characterization of the Product (XXII)

Elemental analysis of the pure TLC homogeneous product (XXII) corresponded to formula $C_{22}H_{42}O_4$. The IR bands at 1735, 1160, 1090 and 1010 cm^{-1} suggested the presence of ester group and

dioxolane ring in the molecule. Its NMR spectrum exhibited a sharp three proton singlet at δ 3.58 which indicated that methyl ester is intact in this product. The signals at 3.96 integrating for two protons and at 3.45 integrating for one proton were due to methylene and methine protons of the ring respectively. Besides these, three other signals were observed at 2.22 m (methylene protons α- to carbonyl), 1.3 br s (chain methylene protons) and 0.9 t (terminal methyl protons). An additional signal at 1.15 as a doublet was due to the methyl protons of the ring. Methylene protons of both the sides of the dioxolane ring were merged in part with chain methylene protons. On the basis of above data the product (XXII) was characterized as methyl 9-(2'-methylethylenedioxolane)octadecanoate. An additional support for the structure of the compound (XXII) was obtained from the study of its mass spectrum.

Its mass spectrum showed the parent ion peak at m/z 371 (M+H). The characteristic intense mass fragments (Scheme 13, Fig. 14) arising from α-cleavages at 243 and 213 established the position of the ring at C9. Other diagnostic mass ions were observed at 339 ($M-OCH_3$), 244 (243+H), 214 (213+H), 211 ($243-CH_3OH$), 113 and 74 (McLafferty). Other salient peaks were observed at 352 ($M-H_2O$), 340 (339+H), 307 ($339-CH_3OH$), 305 ($339-CH_6O$), 185, 169 (185-16), 155, 127 (alkyl fragment α- to ring) and lower mass ions at 71, 59, 55 (base peak) and 43.

Scheme 13


m/z 339
-OCH3
m/z 74 (McLafferty)
m/z 113
M+ 370 (absent)
m/z 213
m/z 243 (base peak)
m/z 155
m/z 185

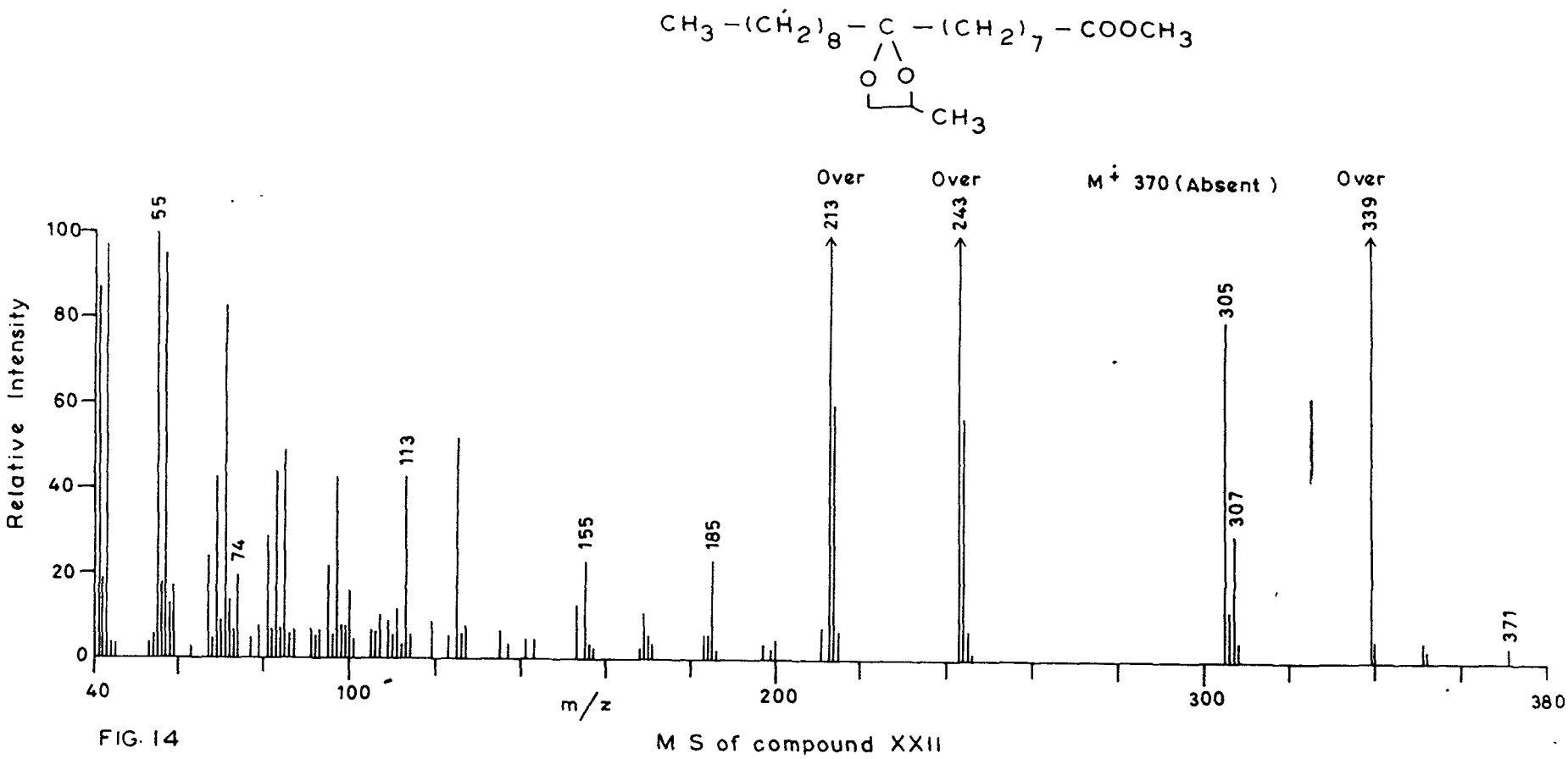


FIG. 14

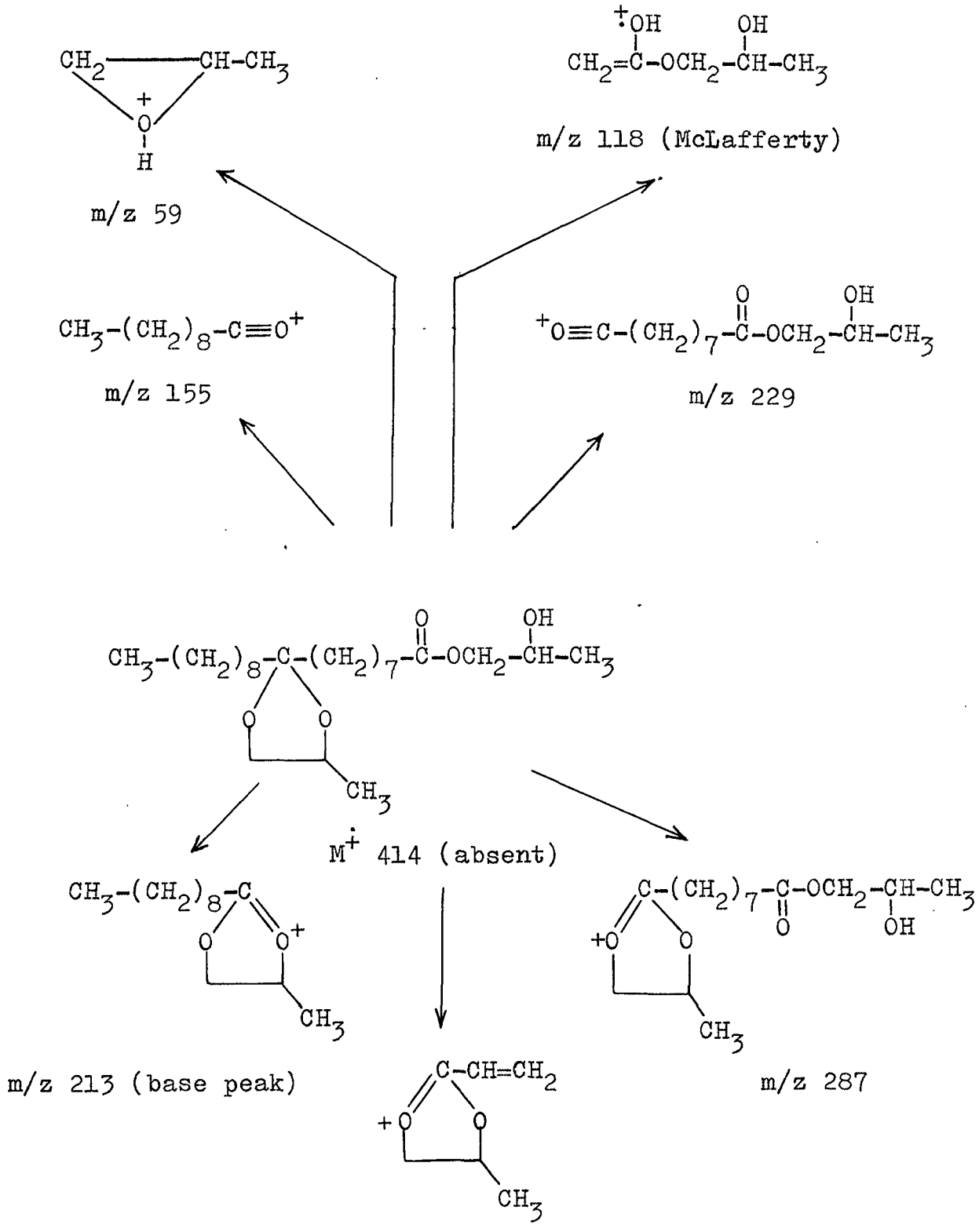
M S of compound XXII

Characterization of the Major Product (XXIII)

Microanalysis of the product (XXIII) corresponded to the composition $C_{24}H_{46}O_5$. Its IR spectrum showed significant bands at 3450 (hydroxyl group), 1730 (ester carbonyl), 1175 and 1090 cm^{-1} (ketal ring vibrations). The NMR of this compound also supported the structure, by showing signals at δ 3.95 m (4H), 3.5 m (2H) for methylene and methine protons of the ring and of hydroxypropyl group respectively, and at 2.3 (3H) attributable to methylene protons α-to carbonyl and one proton of the hydroxyl group, which disappeared after D_2O shake. Signal for methylene protons α-to ring was merged with the broad singlet of chain methylene protons. Methyl protons of the ring and of propyl group appeared at 1.15 as a multiplet and partly merged with chain and terminal methyl protons at 0.9. These data established the structure of the product (XXIII) as 2'-hydroxypropyl-9-(2"-methylethylene-dioxolane)octadecanoate.

Mass spectrum (Scheme 14, Fig. 15) of the compound (XXIII) showed the parent ion peak at m/z 397 (M-OH). The intense peaks at 287 and 213 (base peak) arising from the α-cleavage to the ring confirmed the structure of the compound. Other salient mass ions were found at 345 (M-69), 339 (M-75), 327 (345-OH), 281 (339-C_3H_6O), 288 (287+H), 269 (287-H_2O), 229 (287-C_3H_6O), 214 (213+H), 211 (229-H_2O), 171 (213-C_3H_6), 155, 127, 118, 113, 100, 95, 59, 55, 45 and 43.

Scheme 14


m/z 59
m/z 118 (McLafferty)
m/z 155
m/z 229
M+ 414 (absent)
m/z 213 (base peak)
m/z 287
m/z 113

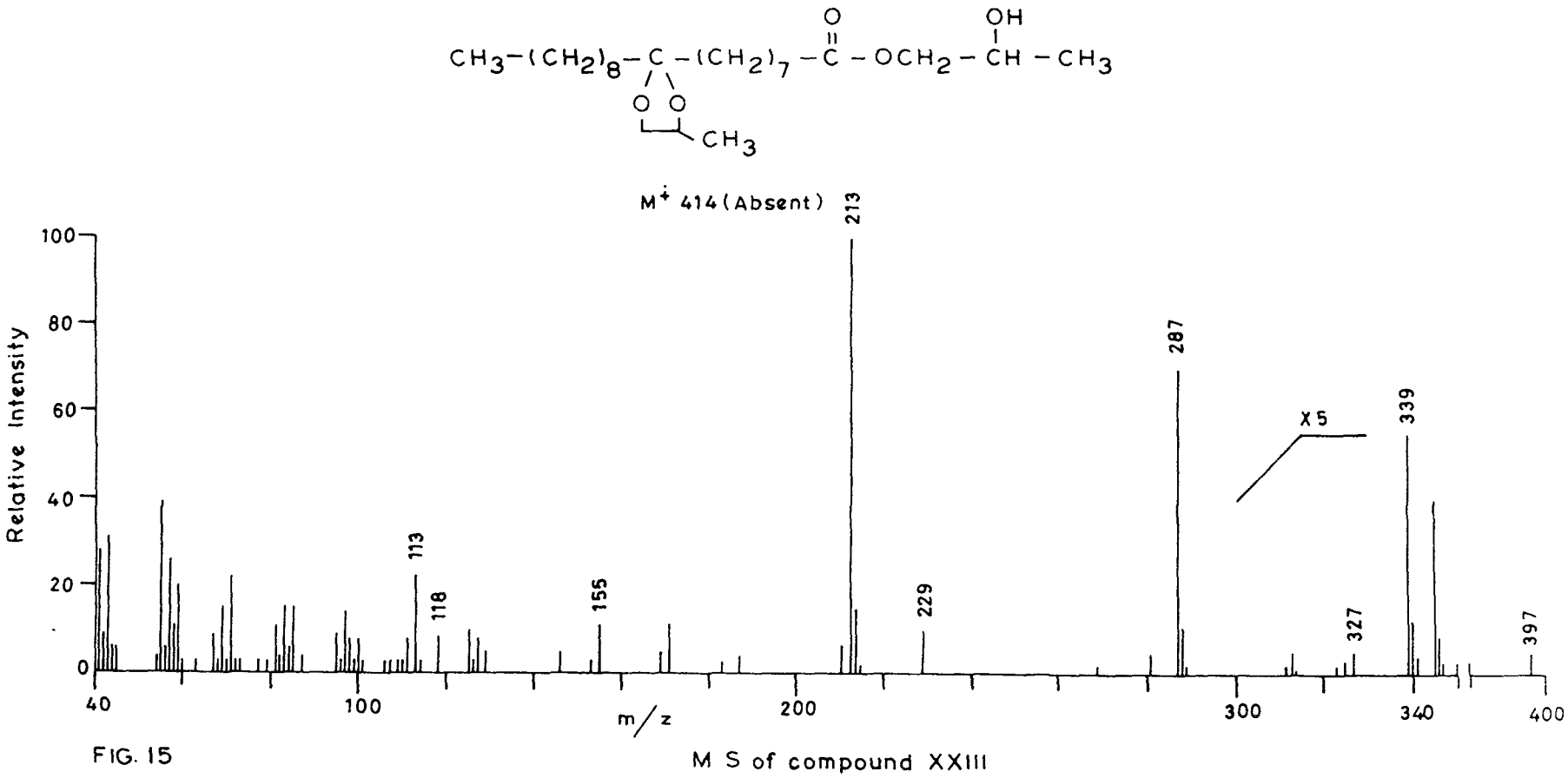


FIG. 15

M S of compound XXIII

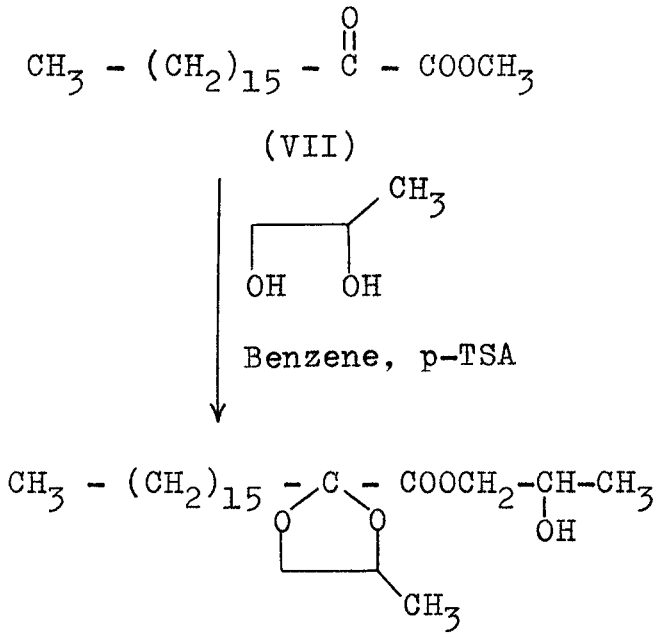
Characterization of the Product (XXIV)

The microanalysis of the solid product (XXIV) agreed well with the formula $C_{21}H_{40}O_4$. Its IR spectrum showed a band at 1695 (oxo),1730 (ester carbonyl) and 3280 cm^{-1} (hydroxyl group). The hydroxyl band suggests the replacement of the methoxy group by 2'-hydroxypropoxy group. In NMR spectrum a signal at δ 2.3 m for six protons (methylene protons α-to oxo function) further confirmed that the oxo group did not react. Other signals appeared at 3.95 for two protons and at 3.5 for one proton (methylene and methine protons respectively), at 2.48 (D_2O exchangeable hydroxylic proton), 1.15 (methyl protons of propyl group) along with usual signals at 1.3 and 0.9. Thus IR and NMR data characterized the product (XXIV) as 2'-hydroxypropyl-9-oxooctadecanoate.

Reaction of 1,2-Propanediol with Methyl 2-oxooctadecanoate(VII)

When methyl 2-oxooctadecanoate was treated with 1,2-propanediol in the same manner as described earlier, only 70% conversion of oxo ester was observed even after prolong refluxing (20 hr) time. This can be explained due to the inductive effect caused by ester carbonyl which makes the reaction site less reactive. In most of the reactions of 2-oxo esters, the less reactivity of oxo group has been attributed due to the close proximity of two functional groups. The reaction product on fractionating over silica gel column gave only

one TLC homogeneous product (XXV).



(XXV)

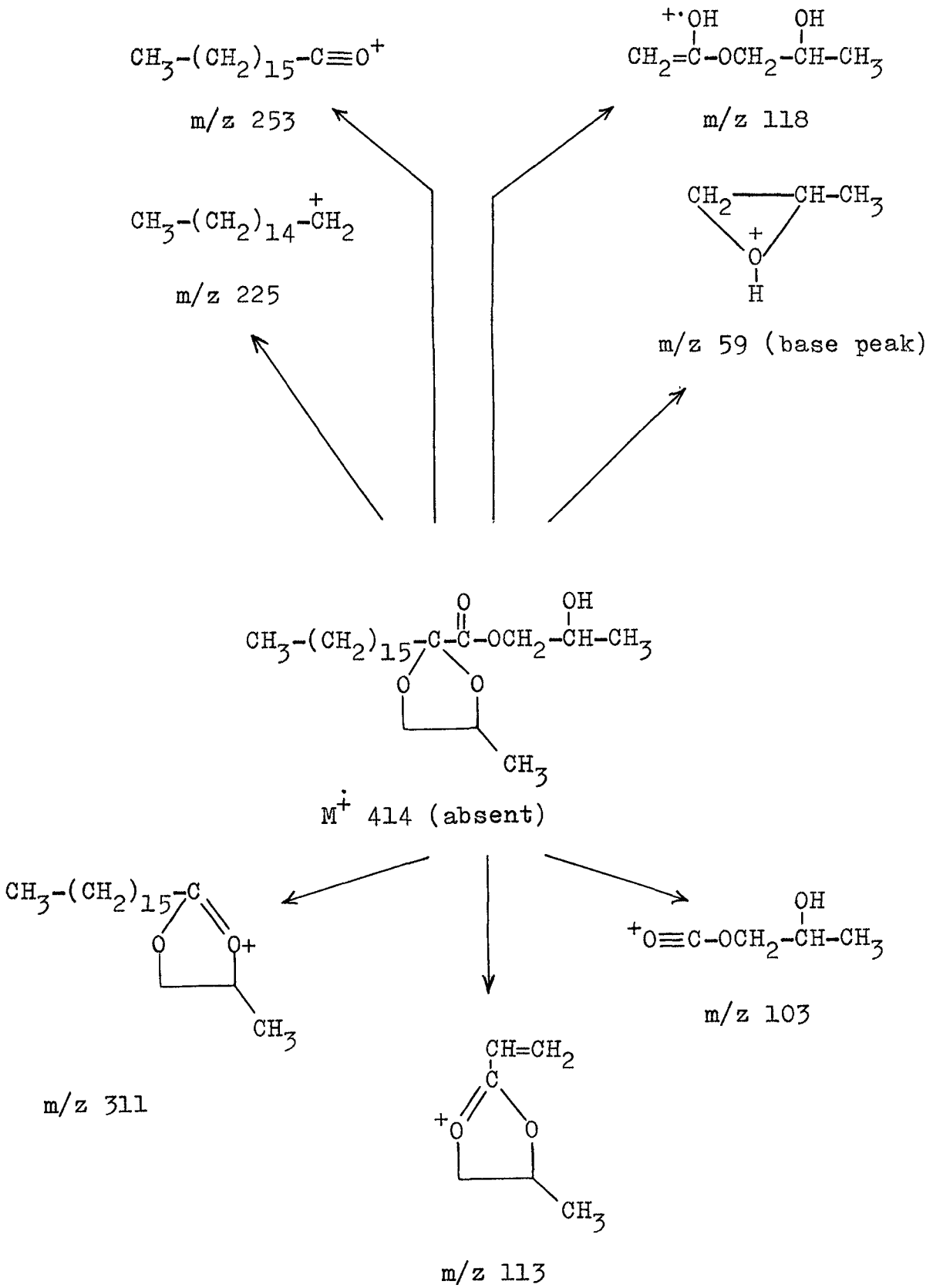
Characterization of the Product (XXV)

The elemental analysis of product (XXV) corresponded to the formula $C_{24}H_{46}O_5$. In its IR spectrum the absence of band at ~1710 cm^{-1} and appearance of bands at 3440, 1170, 1115 and 1070 suggested the incorporation of dioxolane ring and hydroxypropyl group in the molecule. The NMR spectrum was found to be more informative in the elucidation of the structure of XXV. The diagnostic signals as multiplets at δ 3.9 integrating for four protons and at 3.5 integrating for two protons were assignable to the methylene and methine protons of the ring and 2'-hydroxypropoxy group respectively.

The signals at 2.2-2.4 as a broad multiplet integrating for three protons (C3-methylene protons α-to ring and hydroxylic proton, this signal reduces to one third after D_2O shake), 1.3 (chain methylene protons), 1.15 (methyl protons of ring and propoxy group partly merged with chain methylene protons) and 0.9 (terminal methyl protons) supported the structure. Thus the compound was formulated as 2'-hydroxypropyl-2-(2"-methylethylenedioxolane)octadecanoate.

Mass spectrum of XXV confirmed the structure by exhibiting a parent ion peak at m/z 386 (M-28). The characteristic mass ions arising from α-cleavages to ring resulted the alkyl fragment at 225 and ring-containing fragment at 311, thereby establishing the position of dioxolane ring at C3.(Scheme 15, Fig. 16). Other salient peaks were present at 359 (M-55), 312 (311+H), 297 (311-CH_2), 283 (311-C_2H_4), 269 (311-C_3H_6), 271 (269+2H), 253, 243 (271-28), 225 (253-CO), 211 (225-CH_2), 197 (211-CH_2), 113, 103, 59, 55 and 43.

Scheme 15


CH3-(CH2)15-C≡O+
m/z 253
CH3-(CH2)14-CH2+
m/z 225
+·OH OH
CH2=C-OCH2-CH-CH3
m/z 118
CH2 CH-CH3
O+
H
m/z 59 (base peak)
O OH
CH3-(CH2)15-C-C-OCH2-CH-CH3
O O
CH3
M+ 414 (absent)
CH3-(CH2)15-C
O O+
CH3
m/z 311
+O≡C-OCH2-CH-CH3 OH
m/z 103
CH=CH2
C
+O O
CH3
m/z 113

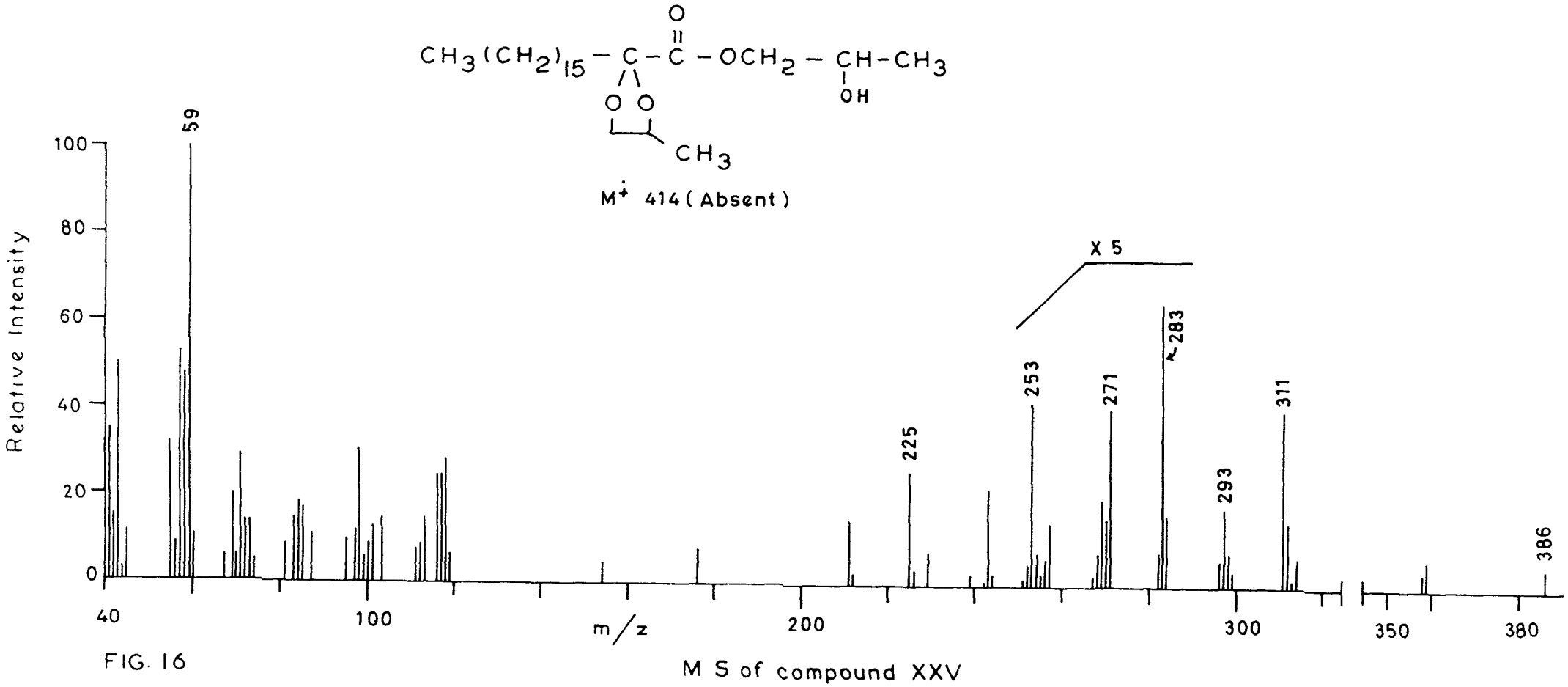


FIG. 16

M S of compound XXV

A comparative study on the mass spectra of toluene-dithiolanes, oxathiolanes and dioxolanes, discussed earlier revealed a number of points worth mentioning. Molecular ion peaks were nonexistent in dioxolanes but were present in oxathiolanes. Dithiolanes showed no definite trends in this respect as is obvious that some of the spectra had and some were deprived of the molecular ion peaks. α-Cleavages to ring were more pronounced and distinctive in the spectra of dioxolanes and dithiolanes in comparison to oxathiolanes. Most of the spectra of dioxolanes had α-cleavage fragment as principal ion. One of the prominent ions in dioxolanes (m/z 113), oxathiolanes (m/z 115) and dithiolanes (m/z 193) was observed due to a simultaneous α-and γ-cleavages to ring with one α-hydrogen loss from this charged species. Such an ion formed is an olefinic cation and thus is stabilizable by heteroatom (oxygen and/or sulfur) and has been identified as characteristic[28] of such type of rings. One more significant ion present was at m/z 55 (CH_2=CH-C≡O+) in dioxolanes and at m/z 71 (CH_2=CH-C≡S+) in dithiolanes. Expectedly, oxathiolanes had both these ions (55, 71) present. An overall critical study of the spectra of these three types of compounds disclosed that dithiolanes provide more informative and easily interpretable spectra than dioxolanes and oxathiolanes. Nevertheless, dioxolanes were better in comparison to oxathiolanes. Various significant ions characteristic of ether and/or thioether were present in the respective spectra.

Chapter 5

Palladium Catalyzed Aromatic Heterocyclic Substitution of Long Chain Olefinic Ester

Theoretical

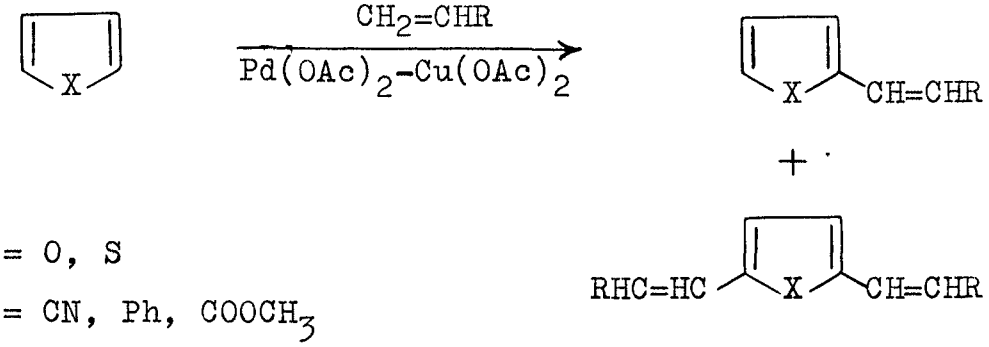
Aromatic heterocyclic fatty derivatives are not much common in natural fats, except few ones. Morris et al.[46] for the first time reported the isolation of 9,12-epoxyoctadec-9, 11-dienoic, a furanoid fatty acid from the seed oil of Exocarpus cupressiformis. Later such type of furanoid fatty acids have also been isolated from the latex of rubber plant[47], soft coral[48] and fish oils[49-52]. Little is known of the function of these compounds, except that these fatty acids may be associated with sexual maturity in fish[49].

The total synthesis of furanoid fatty acids starting from furan synthon viz. furan, furfural, 2-furoic acid, and partial synthesis by the cyclization of unsaturated/oxygenated long chain acids have been described[53-57]. Very recently Lie Ken Jie et al.[58] synthesized pyrrole and thiophene derivatives from dioxostearates.

Fujiwara and coworkers[59-61] reported a novel reaction in which the double bond of the olefin undergoes substitution

reaction with Pd(II) salts and opened a new area of reactions between aromatic compounds (benzene, naphthalene, ferrocene) and short chain olefins. Further, Heck[62] reported that Pd(II) salts are the most generally useful with rhodium and ruthenium salts next best. Acetic acid was found to be the best solvent for these reactions. The yield of addition products increases by the addition of sodium acetate. Pd(II) Acetate has been found more effective catalyst with respect to Pd(II) chloride-sodium acetate. Increasing substitution on the olefin decreases its reactivity.

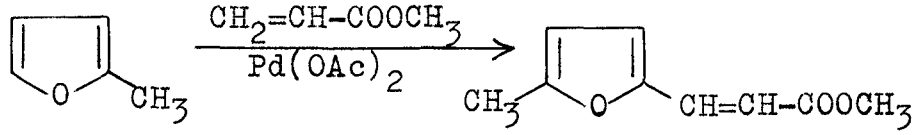
The aromatic heterocycles such as furan, thiophene, pyrrole etc. are the important starting materials for the synthesis of various biologically and physiologically active compounds[63]. However, functionalization of these heterocycles especially introduction of alkenyl groups is difficult and no general method is known for alkenylation except via multistep procedures. In 1979 Fujiwara et al.[64] reported the Pd(II)-catalyzed one step alkenylation of these heterocycles. Recently[65] they developed $Pd(OAc)_2$-$Cu(OAc)_2$ catalyst system for such alkenylation and reported the formation of mono- and dialkenylated products.



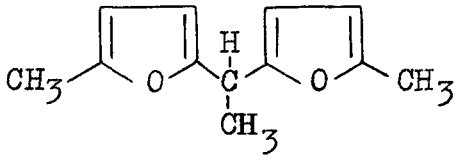
X = O, S

R = CN, Ph, $COOCH_3$

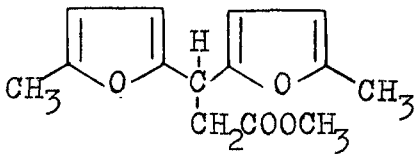
Further they reported[66] that when 2-methyl furan was treated with methyl acrylate, the unsual products noted below were obtained.



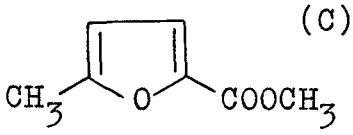
(A) 27%



(B) 22%

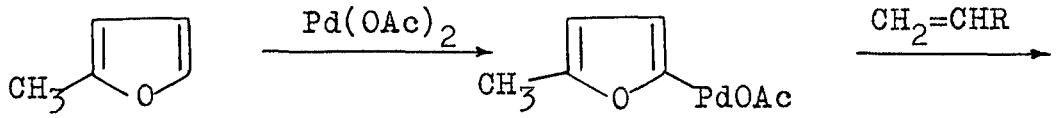


(C) 10%

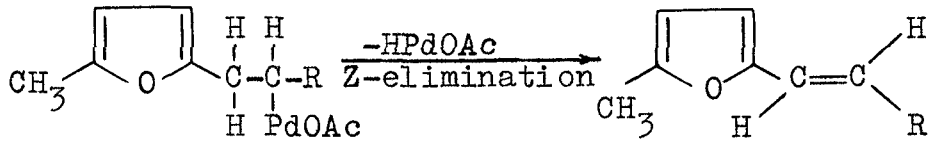


(D) 5%

The formation of B and C in considerable amounts is of particular interest since no such products are obtained with unsubstituted heterocycles. This reaction is stereoselective, occurring exclusively at positions 2- and 5- to give 2-alkenylated and 2,5-dialkenylated heterocycles. The dialkenylated products are formed by further alkenylation of monoalkenylated product. When the substituent on the olefins is bulky such as Ph and $COOCH_3$ groups, the products have E (trans) stereochemistry. It is possible that both E and Z (cis) products are formed initially and Z product undergoes isomerization to give E isomer under the reaction conditions. The following mechanism for this Pd(II)- catalyzed alkenylation was given by Fujiwara.



Furyl-Pd-σ complex



Alkyl-Pd-σ complex E- isomer

R=Ph, $COOCH_3$ etc.

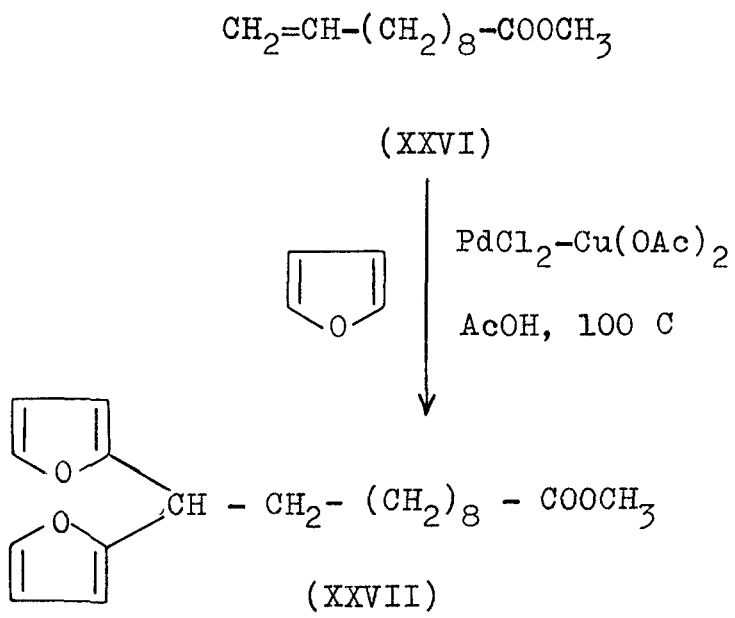
Although the substitution reaction of short chain olefins by aromatic heterocycles in the presence of Pd(II) salts has been studied, scanning of the literature revealed that such type of reactions are not reported in the case of long chain olefinic acids. However, alkyl cadmium or alkyl halides of the required chain length were converted into long chain furanoid derivatives in the presence of various catalysts and furan synthon[53,54]. As a part of our study of the derivatization of aliphatic compounds related to fats, the present work was undertaken to introduce aromatic heterocycles, thiophene, furan, 2-furoic acid and furfuryl alcohol into a terminal olefinic fatty ester by Pd(II)-catalyzed one step substitution reaction.

Discussion

Alkenylation reaction of a terminal olefinic (Methyl 10-undecenoate) ester was studied with furan, furfuryl alcohol, 2-furoic acid, thiophene and pyrrole. In the case of pyrrole the reaction did not occur. With furan an unusual product was obtained. The alkenylation reactions were carried out by the procedure of Fujiwara and coworkers[65] using equimolar amounts of $PdCl_2$, the heterocycles and olefinic ester in a solution of dioxan and acetic acid. The solution was stirred at 100 C. The reaction proceeds catalytically by the use of $Cu(OAc)_2$. Reduced Pd(0) is reoxidized by $Cu(OAc)_2$. Dialkenylated products were not observed in these alkenylation reactions.

Reaction of Furan with Methyl 10-undecenoate (XXVI)

Methyl 10-undecenoate when reacted with $PdCl_2$-$Cu(OAc)_2$ and furan (described in experimental) for 20 hr at 100 C, gave a pale brown colored product. After final work up and fractionation over silica gel column, the product (XXVII) was obtained in 25% yield.



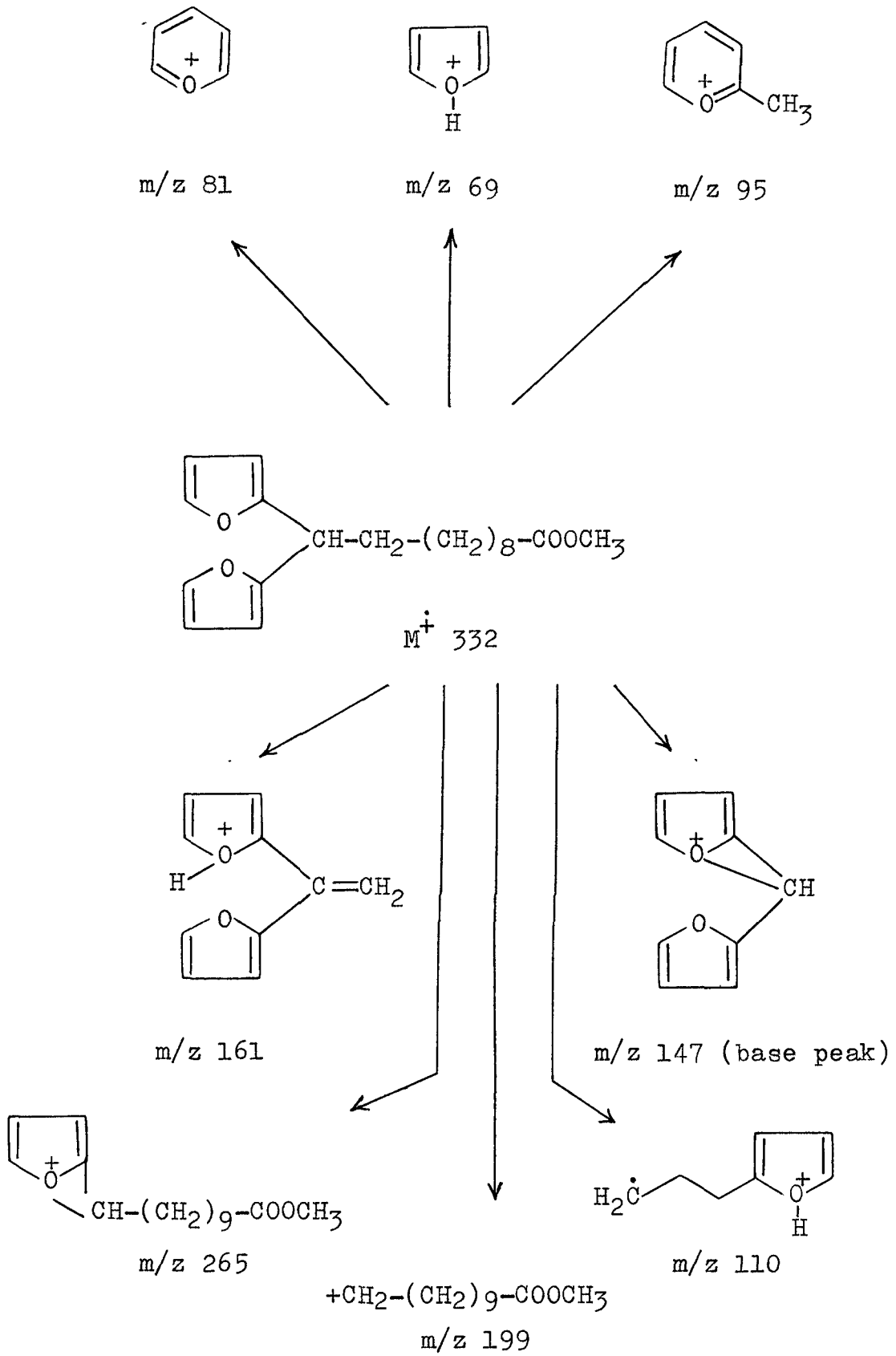
Characterization of the Product (XXVII)

Microanalysis of compound (XXVII) corresponded to the formula $C_{20}H_{28}O_4$. The IR spectrum gave characteristic bands at 3105 (C-H, furan ring), 1610, 1550, 1440 (C=C, furan ring), 1005 (furan ring breathing) and 1735 cm^{-1} (ester carbonyl). Its NMR spectrum showed three characteristic multiplets at δ 7.2 (2H) for C5′-protons, 6.22 (2H) for C4′-protons and 5.8 (2H) for C3′-protons of the furan rings. The greater multiplicity of these signals may be due to the long range coupling. The C11-methine proton appeared at 4.0 as a multiplet. Other usual signals appeared at 3.62 s (3H,-COOC$\underline{H}_3$), 2.25 m (2H, methylene protons α- to carbonyl) and 1.3 br s (chain methylene protons). In the light of above data the compound (XXVII) was formulated as methyl 11,11-(2',2'-difuryl)undecanoate.

Mass spectrum of XXVII (Scheme 16, Fig. 17) strengthened the formulated structure by showing the molecular ion peak at m/z 332 along with the ions at 333 (M+H) and 334 (M+2H). The characteristic mass fragments arising from β- and γ-cleavages to the furan rings at 147 (base peak) and 161 confirmed the attachment of two furan rings with the terminal carbon (C11). The fragments arising from δ- and ϵ-cleavages were also observed at 175 and 189 but the intensities of these ions were very low. The significant peaks due to the presence of furan rings were observed at 95, 81 and 69. In addition to these, other salient peaks were observed at 301 ($M-OCH_3$), 265 (M- furan ring), 233 ($265-CH_3OH$), 199, 185 ($199-CH_2$), 171 ($185-CH_2$), 110, 74 (McLafferty) and 55.

Such unusual type of product was also obtained when Fujiwara and coworkers[66] treated 2-methyl furan with methyl acrylate in the presence of $Pd(OAc)_2$. In an analogy to the Fujiwara's reaction mechanism, it was considered that *in situ* the monoalkenylated product (C) was formed. It could not be isolated because of the higher activity of furan towards $PdCl_2$ forming furyl-Pd-σ complex (A). This complex upon further reaction with monoalkenylated product followed by elimination of HPdCl and hydrogenation[67] gave (XXVII). Formation of XXVII may be rationalized as follows.

Scheme 16


m/z 81
m/z 69
m/z 95
CH-CH2-(CH2)8-COOCH3
M+ 332
m/z 161
m/z 147 (base peak)
CH-(CH2)9-COOCH3
m/z 265
m/z 110
+CH2-(CH2)9-COOCH3
m/z 199

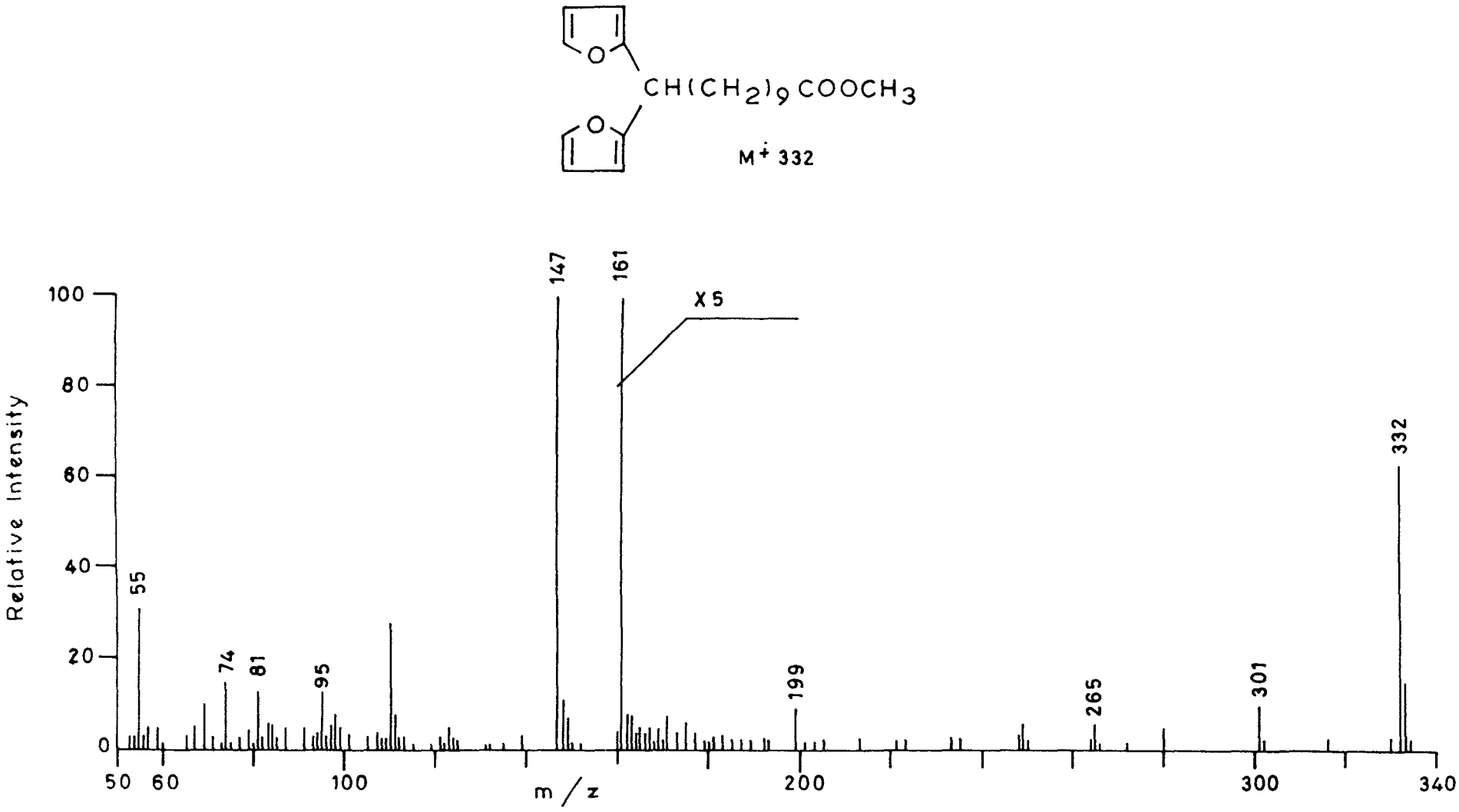
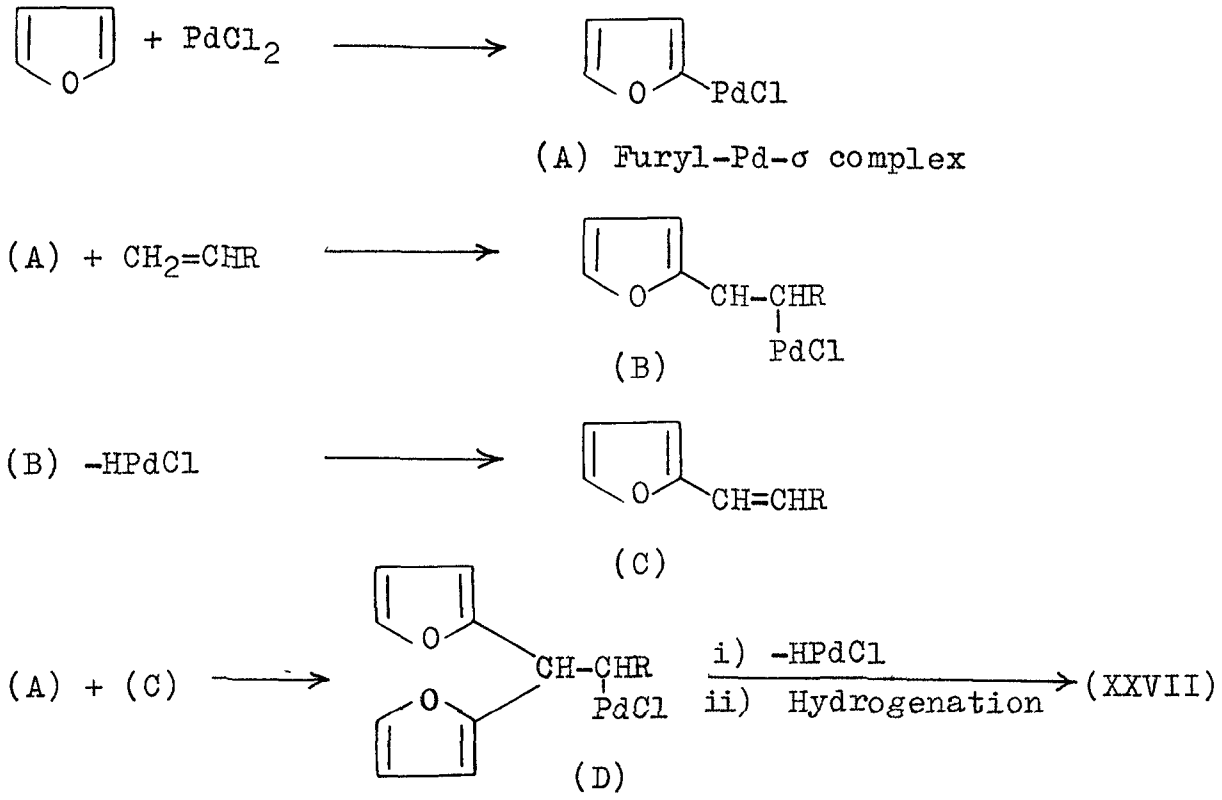


FIG. 17

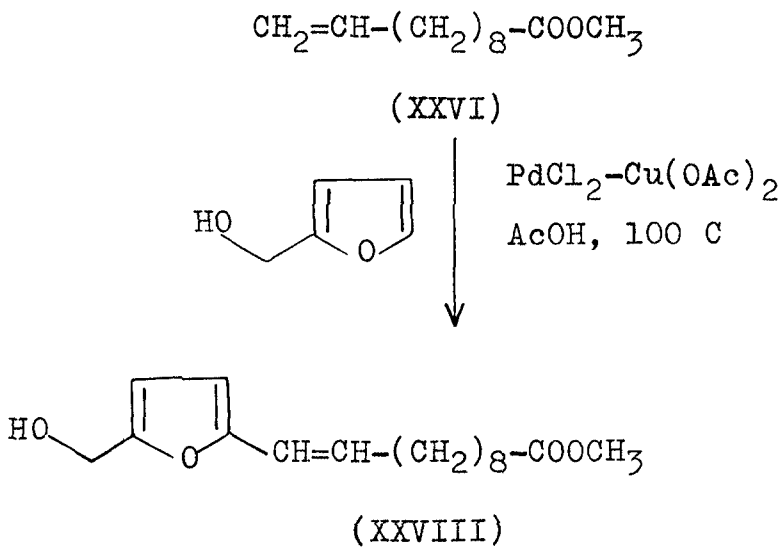
M S of compound XXVII

Mechanism



Reaction of Furfuryl Alcohol with Methyl 10-undecenoate (XXVI)

When furfuryl alcohol was treated with methyl 10-undecenoate and $PdCl_2$-$Cu(OAc)_2$ in the same manner as described earlier, a single product (XXVIII) was obtained in 22% yield after 20 hr.



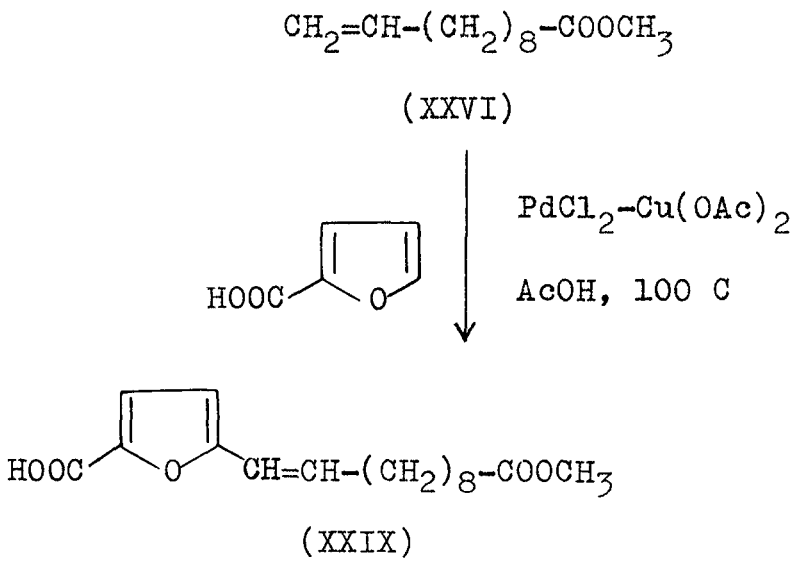
Characterization of the Product (XXVIII)

Elemental analysis of XXVIII corresponded to the formula $C_{17}H_{26}O_4$. Its IR spectrum exhibited strong hydroxyl band at 3440 cm^{-1}. Other significant bands appeared at 3100 (C-H, furan), 1605, 1555, 1440 (C=C, furan) and 1015 (furan ring breathing). A band at 965 showed the presence of a trans double bond in the molecule. The NMR spectrum supported the findings of IR by exhibiting a multiplet centred at δ 6.05 (3H) for C3'-, C4'-protons of furan ring and olefinic proton at C11 to which the furan ring is attached. A multiplet at 5.35 (1H) was ascribable to C10-olefinic proton. Methylene protons attached to hydroxy group appeared at 4.42 and hydroxylic proton at 3.9 along with the usual signals at 3.58 s ($-COOCH_3$), 2.15 m (4H, methylene protons α- to double bond and ester carbonyl) and 1.3 br s (chain methylene protons). Keeping in the view the above data, the product (XXVIII) was formulated as methyl-11-(5'-furfuryl alcohol)-trans-10-undecenoate.

Reaction of 2-Furoic Acid with Methyl 10-undecenoate (XXVI)

2-Furoic acid (α-furoic acid) was allowed to react with methyl 10-undecenoate in the similar fashion as described earlier. A liquid product (XXIX) was obtained after prolong refluxing (40 hr). The low activity may be due to the presence of electron-attracting carboxylic group of 2-furoic acid which

decreases the reactivity of furan ring towards electrophilic substitution at the C5-position of furoic acid.



(XXIX)

Characterization of the Product (XXIX)

The compound (XXIX) was analyzed for $C_{17}H_{24}O_5$. Its IR spectrum showed a band at 3425 (COOH) and two sharp bands at 1735 (ester carbonyl) and 1680 cm^{-1} (acid carbonyl). The characteristic IR bands at 3100 (C-H, furan ring), 1610, 1570, 1430 (C=C, furan ring) and 1010 (furan ring breathing) suggested the substitution of 2-furoic acid in the fatty acid chain. Further a strong band at 970 confirmed the presence of trans double bond. The structure of XXIX was further confirmed by its NMR spectrum. Three characteristic NMR signals were observed as multiplets at δ 7.2 (1H) for C3'-proton, 6.5 (1H) for C4'-proton of furan ring and 6.1 (1H) for C11-olefinic proton of fatty chain. The difference in the chemical shifts

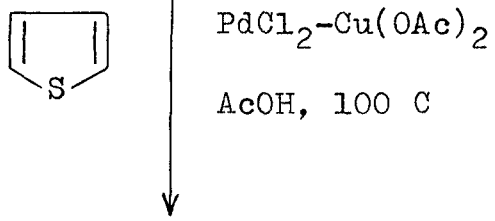
of these protons are due to their unidentical environment, induced by carboxylic group. C10-Olefinic proton appeared as usual at 5.4 as multiplet along with the other signals at 8.6 br s (-COO<u>H</u>), 3.6 s (-COOC<u>H</u>$_3$), 2.25 m (4H, C2-and C9-methylene protons) and 1.3 br s (chain -C<u>H</u>$_2$). These spectral data supported the structure of XXIX as methyl 11-(5'-α-furoic acid)-<u>trans</u>-10-undecenoate.

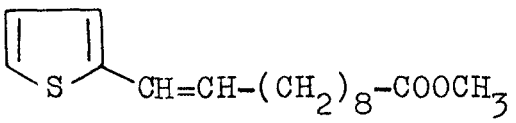
<u>Reaction of Thiophene with Methyl 10-undecenoate (XXVI)</u>

When thiophene was treated with methyl 10-undecenoate for 20 hr in the presence of $PdCl_2$-$Cu(OAc)_2$ as described earlier, a relatively small yield of monoalkenylated product (XXX) was obtained. Alkenylation of thiophene also does not give the dialkenylated product.

$CH_2=CH-(CH_2)_8-COOCH_3$

(XXVI)





(XXX)

Characterization of the Product (XXX)

The compound (XXX) was analyzed for $C_{16}H_{24}O_2S$. As compared to furan the C-H and C=C ring vibrations of thiophene were observed at lower frequency. Its IR spectrum displayed weak bands at 3020 (C-H, thiophene), 1580, 1460 cm^{-1} (C=C, thiophene ring) which confirmed the presence of thiophene ring in the molecule. The other absorptions appeared at 1740 (ester carbonyl) and 970 (trans double bond). Its NMR spectrum corroborated its structure by showing the signals at δ 7.15 as undefined multiplet accountable for one proton of thiophene ring (C5'-proton). Another multiplet at 6.85 for three protons was due to C3'- and C4'-protons of thiophene ring and C11-olefinic proton of the chain. A multiplet for C10-olefinic proton appeared at 5.4. Other usual signals at 3.62 s ($COOCH_3$), 2.25 m (4H, C2- and C9-methylene protons α- to double bond and ester carbonyl) and 1.3 br s (chain methylene protons) were also observed. These data led to the formulation of XXX as methyl 11-(2'-thiophene)-trans-10-undecenoate.

Experimental

All melting points were taken on Kofler apparatus and are uncorrected. Spectroscopic (IR, NMR, Mass) details and thin layer chromatographic procedure have been discussed in Part One. Column chromatography was carried out with silica gel G (60-120 mesh) using 25-30 g per g of material to be separated. Elution was usually effected with petroleum ether with an increase proportions of diethyl ether. Mixture of petroleum ether and diethyl ether will be referred as PE followed by numerals to indicate the relative volumes. Petroleum ether refers to a fraction of bp. 40-60 C. Anhydrous sodium sulfate (Na_2SO_4) was used as drying agent.

The starting materials used were either of commercial grade [10-undecenoic acid, octadec-cis-9-enoic acid and octadecanoic acid] or isolated from natural sources [12-hydroxyoctadec-cis-9-enoic (ricinoleic) and 9-hydroxy-octadec-cis-12-enoic (isoricinoleic) acids from Ricinus communis and Wrightia tinctoria seed oils] respectively,

following Gunstone's partition procedures[68]. Their methyl esters were prepared by the usual method (H^+/MeOH). Solvents for extraction, and reagents and solvents required for reactions were distilled and dried before use.

Preparation of Methyl 10-oxoundecanoate (I)

Mercuric acetate (15.95 g, 50 mmol) was dissolved in a 50:50 mixture of water and tetrahydrofuran (50 ml each) and stirred vigorously[26]. To this reaction mixture 10-undecenoic acid (9.2 g, 50 mmol) was added and stirred for one hr at room temperature to complete the oxymercuration stage. Sodium hydroxide solution (50 ml, 2M) was added, followed by sodium borohydride solution (50 ml, 0.5 M) in sodium hydroxide (3M) for the reduction of the adduct at room temperature. Sodium chloride was added to saturate the water layer and then the mercury was allowed to settle down. The reaction mixture was acidified with dil. HCl to regenerate the acid as well as to destroy the excess of sodium borohydride. Reaction mixture was extracted with diethyl ether, washed with water and dried. Evaporation of solvent followed by crystallization from PE 50 furnished 10-hydroxyundecanoic acid (8.0 g) mp. 49 C(lit. 49.5 C)[26].

10-Hydroxyundecanoic acid (7.8 g) was dissolved in acetone and cooled to ~ 10 C in an ice bath. Jones' reagent[27] (30 ml) was added dropwise with constant stirring over a period of one hr. The mixture was poured in ice cold water, extracted

with diethyl ether, washed with water and dried. Evaporation of the solvent and crystallization from petroleum ether:benzene (1:1, v/v) yielded 10-oxoundecanoic acid (Ia, 6.8 g), mp. 58.5-59 C (lit. 59 C)[26]. Its methyl ester (I) was prepared by catalytic amount of sulfuric acid in methanol.

Preparation of Methyl 12-oxooctadecanoate (II)

Pure 12-hydroxy-octadec-cis-9-enoic acid was isolated from R. communis seed oil by Gunstone partition procedure[68]. This acid on hydrogenation with Pd-C in ethyl acetate at room temperature yielded 12-hydroxyoctadecanoic acid mp. 80-81 C (lit. 82 C)[69]. Jones' oxidation[27] of this saturated hydroxy acid furnished 12-oxooctadecanoic acid mp. 80-81 C(lit. 81.5 C)[69]. On esterification with H^+/CH_3OH, methyl 12-oxooctadecanoate (II), mp. 44-44.5 C (lit. 45 C)[69] was obtained.

Preparation of Methyl 9,10-dioxooctadecanoate (III)

Octadec-cis-9-enoic acid (5.64 g, 20 mmol) containing KOH (11 g) was diluted to 5 litres by water and cooled to 10 C. To this solution $KMnO_4$ (6 g) in ice cold water (250 ml) was added in several portions. After one hr the solution was decolorized with $NaHSO_3$ (30 g) in water (150 ml) followed by 5N HCl (60 ml). The precipitate was filtered off, washed with water and dried. The crude product was dissolved in chloroform(50 ml) which on cooling in ice-bath gave dihydroxy acid(1.35 g). 9,10-Dihydroxy-octadecanoic acid mp. 130 C (lit. 131 C)[70] was obtained upon

crystallization from alcohol.

9,10-Dihydroxyoctadecanoic aicd (6.4 g) was refluxed[29] in ethyl acetate (300 ml), water (200 ml) and N-bromosuccinimide (NBS, 14 g). After 20 min. the bromine was distilled out from ethyl acetate. This ethyl acetate layer was separated, washed with water, concentrated and then diluted with hot methanol (100 ml). The solid product was filtered off. Upon crystallization from alcohol, crystals of 9,10-dioxooctadecanoic acid (IIIa) mp. 84.5 C (lit. 85 C)[71] were obtained in 70% yield. Its esterification (H^+/CH_3OH) gave methyl 9,10-dioxooctadecanoate (III).

(IIIa): IR (Nujol): 1725 (-CO-CO-); NMR: 2.5 m (6H; C2-, C8- and C11-CH_2-), 1.3 and 0.88.

(III) : IR (Nujol): 1735 (-$COOCH_3$); NMR: 3.62 (3H), 2.5 m (6H), 1.3 and 0.88.

Preparation of 9-Oxooctadec-cis-12-enoic Acid (IV)

9-Oxooctadec-cis-12-enoic acid was prepared by the route based on the work of Nichols and Schipper[30].

Strophanthus oil from the seeds of W. tinctoria was repeatedly extracted with light petroleum in a Soxhlet apparatus. The oil (22 g) was refluxed for 2 hr with KOH (4.5 g) dissolved in water (5 ml) and ethanol (250 ml). The unsaponifiable material was removed by diethyl ether extraction

and the mixed fatty acids (20 g) were obtained by acidification of the aqueous layer by dil. HCl followed by diethyl ether extraction. An oxidizing solution of sodium dichromate dihydrate (11 g) in water (15 ml), acetic acid (100 ml) and conc. H_2SO_4 (6 ml) was added to a vigorously stirred solution of mixed fatty acids (15 g) in acetic acid (165 ml) at room temperature and the mixture was stirred for 1 hr. Then the reaction mixture was poured into ice cold water (500 ml) and the solid product was filtered under reduced pressure, washed with cold water and was crystallized from alcohol to afford 9-oxooctadec-cis-12-enoic acid (IV) mp. 44-45 C (3.5 g).

(IV) : Analysis - (Found: C, 72.95; H, 10.85. $C_{18}H_{32}O_3$ requires: C, 72.94; H, 10.87%); IR (Nujol): 1720 (CO), 1705 (COOH); NMR: 5.28 m (-CH=CH-), 2.3 br m (8H), 2.05 m (2H, C14-CH_2-), 1.33 and 0.9; MS: M^+ 296.

Preparation of 9,12-Dioxooctadec-trans-10-enoic Acid (V)

Mixed fatty acids from the seeds of castor (R. communis) were extracted as described for W. tinctoria. An oxidizing solution of sodium dichromate dihydrate (18.2 g) in water (22 ml), acetic acid (160 ml) and conc. H_2SO_4 (10 ml) was quickly added to a vigorously stirred solution of castor fatty acids (25 g) in acetic acid (275 ml) at room temperature. When the temperature had fallen ($\sim$8 C) more oxidizing agent [sodium dichromate dihydrate (20 g), water (100 ml) acetic acid (50 ml)

and conc. H_2SO_4 (10 ml)] was added and the mixture stirred for one hr. With the addition of ice cold water (750 ml) the dioxo acid was precipitated. The product was filtered and crystallized from 90% aqueous ethanol as 9,12-dioxooctadec-trans-10-enoic acid (V, 5 g) mp. 111 C (lit. 112-113 C)[31].

(V) : Analysis - (Found : C, 69.5; H, 9.5. $C_{18}H_{30}O_4$ requires: C, 69.7; H, 9.7%); IR (Nujol): 1685 and 1000; NMR : 6.82 s (-CO-CH=CH-CO-), 2.63 m (-CH_2-CO-CH=CH-CO-CH_2-), 2.32 t (-CH_2-$COOCH_3$), 1.32 and 0.88.

Preparation of Methyl 9-oxooctadecanoate (VI)

Pure 9-hydroxyoctadec-cis-12-enoic acid was isolated from W. tinctoria seed oil by the Gunstone partition procedure[68]. This acid was hydrogenated using Pd-C in ethyl acetate to afford 9-hydroxyoctadecanoic acid, mp. 73-74 C(lit. 75 C)[69] Jones' oxidation[27] of this saturated hydroxy acid yielded 9-oxooctadecanoic acid (VIa) which was crystallized from 80% aqueous alcohol, mp. 81.5-82.5 C (lit. 83 C)[69]. On esterification with H^+/CH_3OH, methyl 9-oxooctadecanoate (VI) was obtained mp. 47-48 C (lit. 47.5 C)[69].

(VIa) : IR (Nujol): 1715 (CO); NMR : 2.27 (6H, C2-, C8- and C1O-CH_2-), 1.3 and 0.9.

(VI) : IR (Nujol): 1715, 1735 ($COOCH_3$); NMR : 3.62 (-$COOCH_3$), 2.25 (6H), 1.3 and 0.9.

Preparation of Methyl 2-oxooctadecanoate (VII)

To a stirring mixture of octadecanoic (stearic) acid (25 g) and red phosphorus (1.2 g), dry bromine (15 ml) was added dropwise at 90 C in a period of 7 hr[72]. The mixture was vigorously stirred during the addition of dry bromine. Heating was continued for 24 hr, then cooled and was poured into cold water and left overnight. The solid product was filtered under reduced pressure, extracted with diethyl ether, washed with aqueous sodium sulfite solution followed by distilled water and dried. Evaporation of the solvent gave 2-bromooctadecanoic acid.

2-Bromo acid (15 g) was refluxed with KOH (6 g) in ethanol (150 ml) for 10 hr. Ethanol was removed under reduced pressure and the reaction mixture was taken in water, acidified with dil. HCl and extracted with diethyl ether. The ethereal layer was washed with water and dried. Evaporation of solvent yielded a mixture of 2-hydroxy- and 2-ethoxy- octadecanoic acids along with some α,β-unsaturated acid. By column chromatography over silica gel, 2-hydroxyoctadecanoic acid was separated as solid product mp. 91-91.5 C (lit. 91 C)[69]. Jones' oxidation of this 2-hydroxy acid afforded 2-oxooctadecanoic acid, mp. 74-74.5 C (lit. 74.5 C)[69]. On esterification (H^+/CH_3OH), methyl 2-oxo-octadecanoate (VII) was obtained, mp. 53.54 C (lit. 54 C)[69].

(VII): IR (CCl_4): 1710 (CO), 1720 ($-\underline{CO}OCH_3$); NMR ($CDCl_3$): 3.6 s($-COO\underline{CH}_3$), 2.4 t ($-\underline{CH}_2COCOOCH_3$), 1.3 and 0.9.

Reaction of Toluene-3,4-dithiol with Methyl 10-oxoundecanoate (I) in BF_3-etherate

A solution of methyl 10-oxoundecanoate (1.07 g, 5 mmol) borontrifluoride-etherate (15 ml) and acetic acid (0.5 ml) was allowed to react with toluene-3,4-dithiol (1.56 g, 10 mmol) at room temperature[13]. The completion of the reaction was observed after 15 min. as evidenced by TLC. Methanol (1 ml) was added to stop the reaction. Reaction mixture was worked up with diethyl ether. The ethereal layer was washed successively with $NaHCO_3$ and water and dried. Evaporation of the solvent afforded an oil. Purification over silica gel column gave VIII (99/; PE-2) as a viscous oil.

(VIII): Analysis - (Found: C, 64.75; H, 8.05. $C_{19}H_{28}O_2S_2$ requires: C, 64.73; H, 7.99%); IR (Neat): 1735 ($\underline{CO}OCH_3$), 3070 (-C=$\underline{C}$-H stretch.; aromatic), 1590 (C=C stretch.; aromatic), 820 (out of plane bending, C-H aromatic); NMR: 6.9 m (3H, aromatic protons), 3.58 s (3H,-COOC$\underline{H}_3$), 2.22 s (3H, methyl protons of toluene), 2.3 m (-C$\underline{H}_2$-COOCH$_3$), 2.09 t (2H, C9-methylene protons α- to dithiolane ring), 1.78 s (3H, terminal methyl protons α- to ring), 1.3 br s (chain methylene protons); MS: M^+ m/z 352.

Reaction of Toluene-3,4-dithiol with Methyl 12-oxooctadecanoate(II)

Toluene-3,4-dithiol (1.56 g, 10 mmol) and methyl 12-oxooctadecanoate (1.56 g, 5 mmol) were allowed to react for 30 min. under

similar conditions as described earlier. Completion of the reaction was evidenced by TLC. Final work up and purification by silica gel column chromatography afforded IX (95%; PE-2) as a liquid product.

(IX): Analysis - (Found: C, 69.25; H, 9.40. $C_{26}H_{42}O_2S_2$ requires: C, 69.29; H, 9.38%); IR (Neat): 3060, 1735, 1585, 810; NMR: 6.87 m (3H, aromatic protons), 3.62 s (3H, $-COOC\underline{H}_3$), 2.26 s (3H, methyl protons of toluene), 2.05 m (6H, C11- and C13-methylene protons α- to ring and C2-methylene protons α-to ester carbonyl), 1.33 br s (chain $-C\underline{H}_2-$), 0.9 t (terminal $-C\underline{H}_3$); MS: Parent ion peak at m/z 365 ($M-C_6H_{13}$).

Reaction of Toluene-3,4-dithiol with 9,10-Dioxooctadecanoic Acid (IIIa)

9,10-Dioxooctadecanoic acid (1.25 g, 4 mmol) was treated with toluene-3,4-dithiol (2.5 g, 16 mmol) for one hr under similar reaction conditions. Purification over silica gel column afforded X (95%; PE-2) as a thick oil.

(X): Analysis - (Found: C, 65.20; H, 7.50. $C_{32}H_{44}O_2S_4$ requires : C, 65.26; H, 7.52%); IR ($CHCl_3$): 3030, 1700, 1590,, 860; NMR: 7.3 m (2H, C5-aromatic proton of two toluene rings), 6.78 m (4H, C2- and C6-aromatic protons of two toluene rings), 2.1 (12H, C2-, C8- and C11-methylene protons merged in part with methyl protons of toluene rings), 1.3 br s (chain-$C\underline{H}_2$), 0.9 t (terminal $-C\underline{H}_3$); MS: Parent ion at m/z 460.

Reaction of Toluene-3,4-dithiol with 9-Oxooctadec-cis-12-enoic Acid (IV)

9-Oxooctadec-cis-12-enoic acid (1.2 g, 4 mmol) and toluene-3, 4-dithol (2.5 g, 16 mmol) in acetic acid (1 ml) and BF_3-etherate (15 ml) were kept overnight. Complete conversion to products was evidenced by TLC. Final work up, as described earlier, and column chromatographic separation afforded XI (85%; PE-5). and XII (10/; PE-10) as oils.

(XI): Analysis- (Found: C, 69.1; H, 8.75. $C_{25}H_{38}O_2S_2$ requires: C, 69.08; H, 8.8/); IR ($CHCl_3$): 3030, 1700, 1620 (C=C, olefin), 1585, 860; NMR: 6.88 br m (3H, aromatic protons), 5.3 m (2H, -CH=CH-), 2.22 s (3H, methyl protons of toluene), 2.08 m (10H, C2-, C8-, C10-, C11- and C14-methylene protons), 1.32 br s (chain $-CH_2-$), 0.9 t (terminal $-CH_3$); MS : M^+ m/z 434.

(XII): Analysis- (Found: C, 65.1; H, 7.8. $C_{32}H_{46}O_2S_4$ requires: C, 65.04; H, 7.83%); IR ($CHCl_3$): 3040, 1710, 1590, 850; NMR: 7.3 m (2H, C5-aromatic protons), 6.88 m (4H, C2- and C6-aromatic protons), 3.1 br m (1H, -CH-S-), 2.08 (12H, C2-, C8-, and C10-methylene protons merged in part with methyl protons of two toluen rings), 1.9 m (1H, -SH), 1.3 br s (chain $-CH_2-$), 0.88 t (terminal $-CH_3$), 9.9 m (-COOH); MS: Parent ion at m/z 432.

Reaction of Toluene-3,4-dithiol with 9,12-Dioxooctadec-trans-10-enoic Acid (V)

9,12-Dioxooctadec-trans-10-enoic acid (1.24 g, 4 mmol) and toluene-3,4-dithiol (3.75 g, 24 mmol) in acetic acid (1 ml) and BF_3-etherate (15 ml) were kept overnight. After complete conversion to products the reaction mixture was worked up. The separation over silica gel column gave XIII (40%; PE-5) and XIV (50%; PE-12).

(XIII): Viscous liquid; Analysis- (Found: C, 65.5; H, 7.25. $C_{32}H_{42}O_2S_4$ requires: C, 65.48; H, 7.2%); IR ($CHCl_3$): 3030, 1620 (C=C, olefin) 1705 (COOH), 1585, 965, 860; NMR: 7.31 m (2H, C2-aromatic protons), 6.9 m (6H, C2- and C6-aromatic protons with two vinylic protons), 2.2 (12H, C2-, C8- and C13-methylene protons merged in part with methyl protons of toluene rings), 1.25 br s (chain $-CH_2-$), 0.9 t (terminal $-CH_3$); MS: Parent ion at m/z 443.

(XIV): Viscous liquid; Analysis- (Found: C, 66.95; H, 8.1. $C_{25}H_{36}O_3S_2$ requires: C, 66.92; H, 8.08%); IR ($CHCl_3$): 3030, 1620 (C=C, olefin), 1710 (COOH), 1690 (COCH=CH), 1590, 960, 860; NMR: 7.4 m (1H, C5-aromatic proton), 6.8 m (4H, C2- and C6-aromatic protons with two vinylic protons), 2.2 (9H, C2-, C8- and C13-methylene protons merged in part with methyl protons of toluene), 1.25 br s (chain $-CH_2-$), 0.9 t (terminal $-CH_3$); MS: Parent ion at m/z 309 (α-cleavage).

Reaction of 10-Oxoundecanoic Acid (Ia) with β-Mercaptoethanol and BF_3-etherate

A solution of 10-oxoundecanoic acid (2.0 g, 10 mmol) and BF_3-etherate (30 ml) was allowed to react with β-mercaptoethanol (3.12 g, 40 mmol) at room temperature[13]. TLC monitoring of the reaction mixture showed that reaction completed within one hr. After adding few drops of methanol to stop the reaction, the content was taken in water and extracted with diethyl ether. The ethereal layer was washed with water and dried. Evaporation of the solvent yielded a viscous oil, which on silica gel column chromatographic separation afforded XV (70%; PE-5) and XVI (20%; PE-20) as oils.

(XV): Analysis- (Found: C, 59.8; H, 9.2. $C_{13}H_{24}O_3S$ requires: C, 59.97; H, 9.28%); IR (Nujol): 1710 (COOH), 1435 (CH_2-S, deformation), 1250 (CH_2-S, Wagging), 1050 (oxathiolane ring)[10]; NMR: 4.15 t (2H,-CH_2-O- of ring), 2.85 t (2H, -CH_2-S- of ring), 2.3 (-CH_2COOH), 1.7 t (2H, methylene protons α- to ring), 1.5 s (3H, terminal methyl protons α- to ring), 1.3 br s (chain -CH_2-), 9.1 br (-COOH); MS: M^+ m/z 260.

(XVI): Analysis- (Found: C, 56.18; H, 9.25. $C_{13}H_{26}O_4S$ requires: C, 56.09; H, 9.4%); IR (Nujol): 3440 (OH), 1715 (COOH), 1455, 1260 (CH_2-S); NMR: 4.22 m (-CH_2-OH), 3.9-3.6 br m (2 x -OH, D_2O exchangeable), 2.85 t (-CH_2-S-), 2.35 m(-CH_2COOH),

1.7 m (methylene protons α- to tertiary carbon), 1.55 s (terminal methyl protons α- to tertiary carbon), 1.25 br s (chain -C<u>H</u>$_2$-).

<u>Reaction of 9-Oxooctadecanoic Acid (VIa) with β-Mercaptoethanol and BF_3-etherate</u>

β-Mercaptoethanol (3.12 g, 40 mmol) and 9-oxooctadecanoic acid (2.98 g, 10 mmol) were allowed to react for 1 hr under the similar conditions as described earlier. Final work up and silica gel column chromatographic separation provided XVII (60%; PE-5) and XVIII (25%; PE-20) as liquids.

(XVII): Analysis- (Found: C, 66.85; H, 10.65. $C_{20}H_{38}O_3S$ requires: C, 66.99; H, 10.67%); IR (Nujol): 1705 (C<u>O</u>OH), 1440, 1255 (CH_2-S), 1045 (oxathiolane ring); NMR: 4.15 t (2H,-C<u>H</u>$_2$-O- of ring), 2.8 t (2H,-C<u>H</u>$_2$-S- of ring), 2.28 m (-C<u>H</u>$_2$COOH), 1.7 m (4H, C8- and C10-methylene protons α- to the oxathiolane ring), 1.32 br s (chain -C<u>H</u>$_2$-), 0.85 t (terminal -C<u>H</u>$_3$); MS: M^+, m/z 358.

(XVIII): Analysis- (Found: C, 63.65; H, 10.6. $C_{20}H_{40}O_4S$ requires: C, 63.79; H, 10.7%); IR (Nujol): 3490 (OH), 1710 (C<u>O</u>OH), 1445, 1250 (CH_2-S); NMR: 4.24 m (-C<u>H</u>$_2$OH), 2.8 t (-C<u>H</u>$_2$-S-), 2.6 br m (2 x -O<u>H</u>, D_2O exchangeable), 2.3 m (-C<u>H</u>$_2$COOH), 1.7 m (4H, C8- and C10-methylene protons α- to tertiary carbon), 1.3 br s (chain -C<u>H</u>$_2$-), 0.9 t (terminal -C<u>H</u>$_3$).

Reaction of Methyl 9,10-dioxooctadecanoate (III) with β-Mercaptoethanol, BF_3-etherate and Acetic Acid

Methyl 9,10-dioxooctadecanoate (3.26 g, 10 mmol) was dissolved in acetic acid (5 ml) and treated with β-mercaptoethanol (3.12 g, 40 mmol) and BF_3-etherate (15 ml) and left at room temperature for 4 hr. Methanol (0.5 ml) was added and the reaction mixture was poured into water and extracted with diethyl ether. The ethereal layer was washed successively with water, aqueous solution (5%) of sodium bicarbonate and water and dried. Evaporation of solvent and purification by column chromatography yielded an oily product XIX (80%; PE-10). (XIX): Analysis- (Found: C, 65.15; H, 9.84. $C_{21}H_{38}O_4S$ requires: C, 65.25; H, 9.9%); IR (Nujol): 1735 ($\underline{C}OOCH_3$), 1715 ($\underline{C}OCH_2$), 1435, 1230 (CH_2-S), 1025 (oxathiolane ring); NMR: 4.12 t (2H, -$C\underline{H}_2$-O- of the ring), 3.6 s (-COOC$\underline{H}_3$), 2.72 t (2H, -$C\underline{H}_2$-S- of the ring), 2.3 m (4H, methylene protons α- to oxo and ester carbonyl), 1.65 t (2H, methylene protons α- to oxathilane ring), 1.3 br s (chain -$C\underline{H}_2$-), 0.9 t (3H, terminal -$C\underline{H}_3$); MS: M^+, m/z 386.

Reaction of 1,2-Propanediol with Methyl 10-oxoundecanoate (I) in presence of p-TSA

1,2-Propanediol (10.26 g, 135 mmol) and dry benzene (100 ml) were refluxed in a Dean Starks' apparatus to remove the traces of water. To this solution, methyl 10-oxoundecanoate (2.14 g,

10 mmol) was added followed by p-toluenesulfonic acid (p-TSA, 100 mg). A 2 hr reflux of the reaction mixture showed the complete conversion of the reactant on the TLC plate. Benzene was evaporated under reduced pressure and the reaction mixture was worked up with diethyl ether. The ethereal layer was washed with 5% aqueous solution of sodium bicarbonate followed by water and dried. Evaporation of the solvent gave two TLC homogeneous products, which were purified on silica gel column, XX (75%; PE-8) and XXI (20%; PE-10).

(XX): Oil; Analysis-(Found: C, 64.49; H, 10.15. $C_{17}H_{32}O_5$ requires: C, 64.53; H, 10.18%); IR (Neat): 3470 (OH), 1740 (-$\underline{C}\underline{O}OCH_2$-), 1170, 1100, 1050 (C-O); NMR: 3.95 m (4H, C1'- and C1"-methylene protons), 3.5 m (2H, C2'- and C2"-methine protons), 2.75 br m (1H, -O$\underline{H}$, D_2O exchangeable), 2.25 m (2H,-C$\underline{H}_2$COOCH$_2$-), 1.23 (terminal methyl and methylene protons α- to ring, partly merged with chain-C$\underline{H}_2$ protons), 1.15 (2 x C$\underline{H}_3$); MS: Parent ion at m/z 301 ($M-CH_3$).

(XXI): mp. 56-57 C; Analysis- (Found: C, 65.1; H, 10.11. $C_{14}H_{26}O_4$ requires: C, 65.09; H, 10.12%); IR (CCl_4): 3440 (OH), 1730 (-$\underline{C}\underline{O}OCH_2$-), 1695 ($CH_3\underline{C}\underline{O}CH_2$-), 1160, 1095, 1010 (C-O); NMR: 3.9 d (2H, C1'-methylene protons), 3.55 m (1H, C2'-methine proton), 2.55 br m (1H,-O$\underline{H}$), 2.35 m (4H, C2- and C9-methylene protons), 2.08 s (terminal C$\underline{H}_3$-,α- to oxo group), 1.15 d (3H, C3'-methyl protons merged in part with

chain methylene protons), 1.3 br s (chain-C<u>H</u>$_2$-);·MS: $M^{\dot{+}}$,m/z 258.

<u>Reaction of 1,2-Propanediol with Methyl 9-oxooctadecanoate (VI)</u>

Reaction of 1,2-propanediol (10.26 g, 135 mmol) with methyl 9-oxooctadecanoate (3.12 g, 10 mmol) was carried out as described earlier but refluxed for 16 hr. Final work up and purification on silica gel column gave three products, XXII (15%; PE-4), XXIII (60%; PE-8) and XXIV (20%; PE-10).

(XXII): Oil; Analysis- (Found: C, 71.4; H, 11.45. $C_{22}H_{42}O_4$ requires: C, 71.31; H, 11.41%); IR (Neat): 1735 (-C<u>O</u>OCH$_3$), 1160, 1090, 1010 (C-O); NMR: 3.96 m (2H, C1"-methylene protons), 3.58 s (-COOC<u>H</u>$_3$), 3.45 m (1H, C2"-methine proton), 2.22 m (-C<u>H</u>$_2$COOCH$_3$), 1.3 br s (chain -C<u>H</u>$_2$-), 1.15 d (-C<u>H</u>$_3$ protons of the ring), 0.9 t (terminal -C<u>H</u>$_3$); MS: m/z 371 (M+H).

(XXIII): Oil; Analysis- (Found: C, 69.55; H, 11.2. $C_{24}H_{46}O_5$ requires: C, 69.53; H, 11.17%); IR (Neat): 3450 (OH), 1730 (-C<u>O</u>OCH$_2$-), 1175, 1090 (C-O); NMR: 3.95 m (4H, C1'- and C1"-methylene protons), 3.5 br m (2H, C2'- and C2"-methine protons), 2.3 br m (3H, C2-methylene and -CH-O<u>H</u> protons), 1.25 br s (chain -C<u>H</u>$_2$-), 1.15 m (6H, 2 x -C<u>H</u>$_3$, merged in part with chain -C<u>H</u>$_2$-), 0.9 t (terminal -C<u>H</u>$_3$); MS: Parent ion at m/z 397 (M-OH).

(XXIV): mp. 76-77 C; Analysis- (Found: C, 70.81; H, 11.32. $C_{21}H_{40}O_4$ requires: C, 70.75; H, 11.3%); IR (CCl_4): 3280 (OH), 1730 (-COOCH$_2$-), 1695 (CH$_2$COCH$_2$), 1175, 1105, 1080, 1030(C-O); NMR: 3.95 m (2H, C1'-methylene protons), 3.5 m (1H, C2'-methine proton), 2.48 s (1H, -CH-OH), 2.3 m (6H, C2-, C8- and C10-methylene protons), 1.3 br s (chain -CH$_2$-), 1.15 (3H, C3'-methyl protons merged in part with chain methylene protons), 0.9 t (terminal -CH$_3$).

Reaction of 1,2-Propanediol with Methyl 2-oxooctadecanoate(VII)

Reaction of methyl 2-oxooctadecanoate (3.12 g, 10 mmol) with 1,2-propanediol (10.26 g, 135 mmol) was carried out under the similar conditions described earlier, except the prolong refluxing time (20 hr). Final work up afforded the oily product, which on column chromatographic purification yielded XXV (70%; PE-10).

(XXV): Analysis- (Found: C, 69.59; H, 11.21. $C_{24}H_{46}O_5$ requires: C, 69.53; H, 11.17%); IR (Neat): 3440 (OH), 1735 (-COOCH$_2$), 1170, 1115, 1070 (C-O); NMR: 3.9 m (4H, C1'- and C1"-methylene protons), 3.5 m (2H, C2'- and C2"-methine protons), 2.3 br m (3H, C3-methylene protons and -CH-OH*, D$_2$O* exchangeable), 1.3 br s (chain -CH$_2$-), 1.15 m (6H, 2 x CH$_3$, merged in part with chain -CH$_2$-), 0.9 t (terminal -CH$_3$); MS: m/z 386 (M-C$_2$H$_4$).

Reaction of Furan with Methyl 10-undecenoate (XXVI)

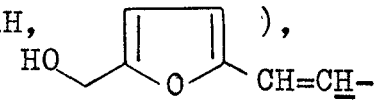
In a round bottom flask (250 ml) containing a magnetic stirring bar, methyl 10-undecenoate (3.96 g, 20 mmol), furan (1.3 g, 20 mmol) $PdCl_2$ (90 mg, 0.5 mmol), $Cu(OAc)_2$ (7.98 g, 40 mmol), dioxan (150 ml) and acetic acid (15 ml) were added[65]. The solution was stirred for 20 hr at 100 C (no further conversion of reactant was noticed after this period). The reaction mixture was filtered to remove the Pd and Cu metals. The filterate was poured into water and the mixture was extracted with diethyl ether. The ethereal extract was washed with excess of water, aqueous sodium bicarbonate (1%) to remove the excess of acid, water and dried (Na_2SO_4). Evaporation of the solvent afforded an oil. Purification over silica gel column gave XXVII (25%; PE-5) as an oily product.

(XXVII): Analysis- (Found: C, 72.35; H, 8.55. $C_{20}H_{28}O_4$ requires: C, 72.26; H, 8.48%); IR (Neat): 3105 (C-H, furan ring), 1610, 1550, 1440 (C=C, furan ring), 1735 ($\underline{C}OOCH_3$), 1005 (furan ring breathing); NMR: 7.2 m (2H), 6.22 m (2H), 5.8 m (2H), 4.0 m (C11- methine proton), 3.62 s ($-COOC\underline{H}_3$), 2.25 m (2H, C2-methylene protons), 1.3 br s (chain $-C\underline{H}_2-$); MS: M^+ m/z 332.

Reaction of Furfuryl Alcohol with Methyl 10-undecenoate (XXVI)

Reaction of equimolar quantity of methyl 10-undecenoate (3.96 g, 20 mmol) and furfuryl alcohol (1.96 g, 20 mmol) in

dioxan (150 ml) and acetic acid (15 ml) in the presence of $PdCl_2$ (90 mg, 0.5 mmol) and $Cu(OAc)_2$ (7.98 g, 40 mmol) for 20 hr at 100 C afforded the TLC homogeneous product along with starting methyl 10-undecenoate. The reaction mixture was worked up as described before. Purification over silica gel column gave XXVIII (22%; PE-10) as liquid product.

(XXVIII): Analysis- (Found: C, 69.4; H, 8.9. $C_{17}H_{26}O_4$ requires: C, 69.37; H, 8.89%); IR (Neat): 3440 (OH), 3100, 1605, 1555, 1440, 1015 (furan ring), 1735 (C<u>O</u>OCH$_3$), 965 (<u>trans</u> double bond); NMR: 6.05 m (3H, C3'-,C4'-protons of furan ring and C11-olefinic proton), 5.35 m (1H, ), 4.42 m (-C<u>H</u>$_2$-OH), 3.9 m (-CH$_2$-O<u>H</u>), 3.58 s (3H, -COOC<u>H</u>$_3$), 2.15 m (4H, methylene protons α- to double bond and ester carbonyl), 1.3 br s (chain -C<u>H</u>$_2$-).

<u>Reaction of 2-Furoic Acid with Methyl 10-undecenoate (XXVI)</u>

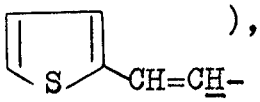
Treatment of methyl 10-undecenoate (3.96 g, 20 mmol) with 2-furoic acid (2.24 g, 20 mmol) under the same conditions except a longer duration of stirring (40 hr) provided XXIX (25%; PE-8) as an oily product.

(XXIX): Analysis- (Found: C, 66.25; H, 7.8. $C_{17}H_{24}O_5$ requires: C, 66.22; H, 7.84%); IR (Neat): 3425 (COO<u>H</u>), 3100, 1610, 1570, 1430 and 1010 (furan ring), 1735 (C<u>O</u>OCH$_3$), 1680 (C<u>O</u>OH), 970 (C=C, <u>trans</u>); NMR: 7.2 m (C3'-proton of furan ring)

6.5 m (C4'-proton of furan ring), 6.1 m (1H, C11- olefinic proton), 5.4 m (1H, C10- olefinic proton), 8.6 br s (-COO<u>H</u>), 3.6, 2.25, 1.3.

<u>Reaction of Thiophene with Methyl 10-undecenoate (XXVI)</u>

Stirring of methyl 10-undecenoate (3.96 g, 20 mmol) and thiophene (1.68 g, 20 mmol) in the solvent dioxan-acetic acid at 100 C for 20 hr as in the case of furan, afforded XXX, (30%; PE-3) as a liquid product.

(XXX): Analysis- (Found: C, 68.55; H, 8.65. $C_{16}H_{24}O_2S$ requires: C, 68.53; H, 8.62%); IR (Neat): 3020 (C-H, thiophene), 1740 (-<u>C</u>OOCH$_3$), 1580, 1460 (C=C, thiophene), 970 (<u>trans</u> double bond); NMR: 7.15 m (1H, C5'-thiophene proton), 6.85 m (3H, C3'-, C4'-thiophene protons and C11-olefinic proton), 5.4 m (1H, 

), 3.62 s (3H, -COOC<u>H</u>$_3$), 2.25 (4H, C2- and C9-methylene protons α- to double bond and ester carbonyl), 1.3 (chain -C<u>H</u>$_2$-).

<u>Reaction of Pyrrole with Methyl 10-undecenoate (XXVI)</u>

A mixture containing pyrrole (1.34 g, 20 mmol), methyl 10-undecenoate (3.96 g, 20 mmol), $PdCl_2$ (90 mg, 0.5 mmol), $Cu(OAc)_2$ (7.98 g, 40 mmol), dioxan (150 ml) and acetic acid (15 ml) was stirred at 100 C for four days. After usual work up, the reaction regenerated only original methyl 10-undecenoate (XXVI).

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2. Derivatization of Keto Fatty Acids Part V. Synthesis and Characterization of 1,3-Dioxolanes.
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4. Derivatization of Keto Fatty Acids Part IX. Synthesis and Characterization of Oxathiolanes.
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5. Characterization and Measurement of HBr-reacting acids in Abelmoschus moschatus seed oil.
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6. Synthesis of Substituted Ketals from Oxo Fatty Acids.
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7. Reaction of INO_3 with Hydroxyolefinic Fatty Acids.
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